

ENDOSCOPY AND DIAGNOSTIC IMAGING

Part 1

**Skin, Nail and Mouth Changes in GI Disease;
Esophagus; Stomach; Small intestine; Pancreas**

COMPLEMENTING GI PRACTICE REVIEW

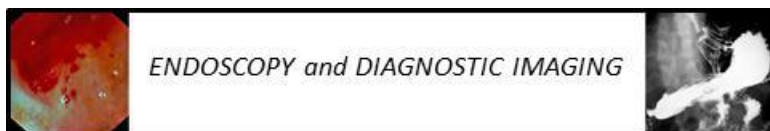
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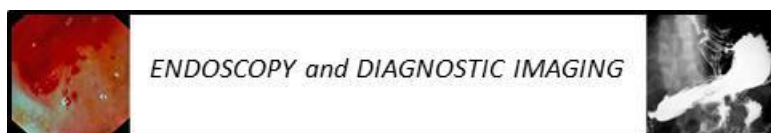
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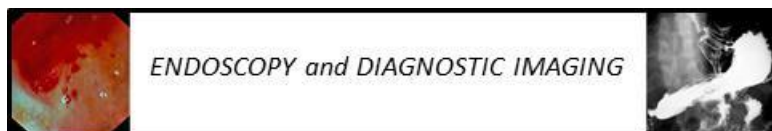
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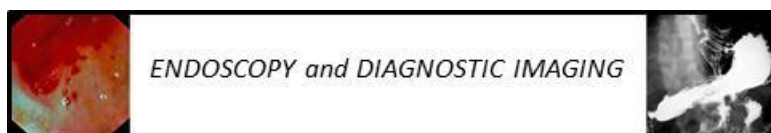
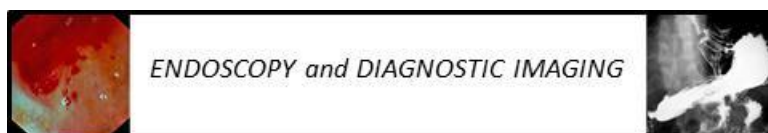


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Endoscopy and Diagnostic Imaging and the CANMED Objectives

Medical expert

The discussion of complex cases provides the participants with an opportunity to comment on additional focused history and physical examination. They would provide a complete and organized assessment. Participants are encouraged to identify key features, and they develop an approach to problem-solving.

The case discussions, as well as the discussion of cases around a diagnostic imaging, pathological or endoscopic base provides the means for the candidate to establish an appropriate management plan based on the best available evidence to clinical practice. Throughout, an attempt is made to develop strategies for diagnosis and development of clinical reasoning skills.

Communicator

The participants demonstrate their ability to communicate their knowledge, clinical findings, and management plan in a respectful, concise and interactive manner. When the participants play the role of examiners, they demonstrate their ability to listen actively and effectively, to ask questions in an open-ended manner, and to provide constructive, helpful feedback in a professional and non-intimidating manner.

Collaborator

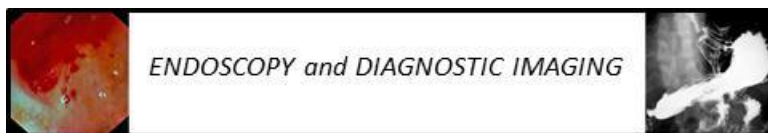
The participants use the “you have a green consult card” technique of answering questions as fast as they are able, and then to interact with another health professional participant to move forward the discussion and problem solving. This helps the participants to build upon what they have already learned about the importance of collegial interaction.

Manager

Some of the material they must access demands that they use information technology effectively to access information that will help to facilitate the delineation of adequately broad differential diagnoses, as well as rational and cost effective management plans.

Health advocate

In the answering of the questions and case discussions, the participants are required to consider the risks, benefits, and costs and impacts of investigations and therapeutic alliances upon the patient and their loved ones.



Scholar

By committing to the pre- and post-study requirements, plus the intense three day active learning Practice Review with colleagues is a demonstration of commitment to personal education. Through the interactive nature of the discussions and the use of the “green consult card”, they reinforce their previous learning of the importance of collaborating and helping one another to learn.

Professional

The participants are coached how to interact verbally in a professional setting, being straightforward, clear and helpful. They learn to be honest when they cannot answer questions, make a diagnosis, or advance a management plan. They learn how to deal with aggressive or demotivated colleagues, how to deal with knowledge deficits, how to speculate on a missing knowledge byte by using first principals and deductive reasoning. In a safe and supportive setting they learn to seek and accept advice, to acknowledge awareness of personal limitations, and to give and take 360⁰ feedback.

Knowledge

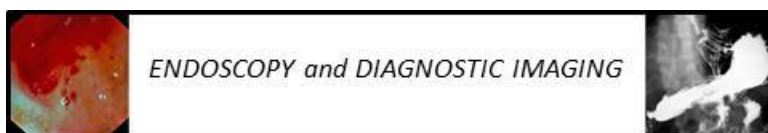
The basic science aspects of gastroenterology are considered in adequate detail to understand the mechanisms of disease, and the basis of investigations and treatment. In this way, the participants respect the importance of an adequate foundation in basic sciences, the basics of the design of clinical research studies to provide an evidence-based approach, the designing of clinical research studies to provide an evidence-based approach, the relevance of their management plans being patient-focused, and the need to add “compassionate” to the Three C’s of Medical Practice: competent, caring and compassionate.

“They may forget what you said, but they will never forget how you made them feel.”

Carl W. Buechner, on teaching.

“With competence, care for the patient. With compassion, care about the person.”

Alan B. R. Thomson, on being a physician.

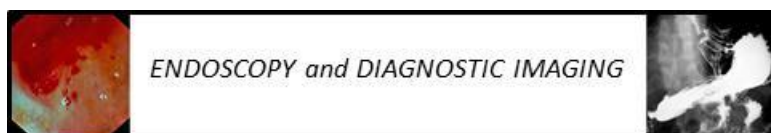


Prologue

Like any good story, there is no real beginning or ending, just an in-between glimpse of the passing of time, a peek into a reality of people's minds, thoughts, feelings, and beliefs. The truth as I know it has a personal perspective which drifts into the soul of creation. When does life begin, when does an idea become conceived, when do we see love or touch reality? A caring, supportive, safe, and stimulating environment creates the holding blanket, waiting for the energy and passion of those who dream, invent, create – disrupt the accepted, challenge the conventional, ask the questions with forbidden answers. Be a child of the 60's. Just as each of us is a speck of dust in the greater humanity, the metamorphosis of the idea is but a single sparkle in the limitlessness of the Divine Intelligence. We are the ideas, and they are us. No one of us is truly the only parent of the idea, for in each of us is bestowed the intertwined circle of the external beginning and the end....

....during a visit to the Division of Gastroenterology at the University of Ottawa several years ago, the trainees remarked how useful it would be to have more than two hours of learning exchange, a highly interactive tutorial with concepts, problem solving, collegial discussion, the fun and joys of discovery and successes. Ms. Jane Upshall of BYK Canada (Atlanta, Nycomed), who had sponsored two of these visiting Professorships, encouraged the possibility of the development of a longer program. Her successor, Lynne Jamme-Vachon, supported the initial three day educational event for the trainees enrolled in the GI training program at the University of Ottawa. With her entrepreneurial foresight, wisdom, and enthusiasm, the idea began. Lynne's commitment to an event which benefited many of the future clinicians, who will care for ourselves and our loved ones, took hold. Then, thanks to the GI program directors in Ottawa and the University of Western Ontario, Nav Saloojee and Jamie McGregor, more trainees were exposed, future GI fellows talked with other trainees, and a grass roots initiative began. Had it not been for Nav and Jamie's willingness to take a risk on something new, had they not believed in me, then there would have been no further outreach. Thank you, Lynne, Nav, and Jamie. You were there at the beginning. I needed you.

By 2008, all but one GI program in the country gave their trainees time off work to participate in the three day event, GI Practice Review (GI-PR). The course is 90% unsponsored, and is gratis to the participants, (except for the



cost of their enthusiastic participation!) I am happy to give back to the subspecialty that gave me so much for 33 years. I hope GI-PR is helpful to all trainees. I know that from these future leaders there will arise those who will continue to dedicate and donate their time, energy, and ability to the betterment of those who contribute to the continued improvement of our medical profession. The clinicians, the teachers, the researchers.

In the short span of six years, more than 250 fellows, coming from all the 14 training programs in Canada, have participated in the small group sessions in the GI practice review. I thank the training program directors who have supported GI-PR. Special appreciation as well to their many staff physicians who worked without their trainees for the three days of each program.

The idea for the electronic and hard copy summary of the “list of facts” came from the trainees who wished for an aide memoir. But the GI-PR is about more than lists and facts - it is about problem formulation, case discussions, review of endoscopy, histopathology, motility, diagnostic imaging. It is about having fun working together to learn. The subterfuge to gain interest in the basic sciences is the use of clinical scenarios to show the way to the importance of first principles. While the lists are here, the experience is in the performance.

The child will grow, the images will expand, the learning of all aspects of our craft will develop and flourish amongst persons of good will. Examinations will become second nature, as each clinical encounter, each person, each patient, becomes our test, the determination of clinical competence, of caring, of compassion. May these three C's become part of each of our live's narrative. And from this start comes Capstone Academic Publishing, an innovation for the highest quality and value in educational material, made available at cost, speaking in tongues, in the languages of many cultures, with the dialect of the true North strong and free, so that knowledge will be free at last.

Outstanding medical practice and true dedication to those from whom we receive both a privilege and pleasure of care, comes from much more than the GI-PR can give you, much more than Q & As, descriptions of diagnostic imaging or endoscopy stills or videos, histopathology or motility. True, we need all of these to jump over a very high bar. But to be a truly outstanding physician, you need to care for and care about people, and you must respect the dignity and rights of all others. You must strike a balance

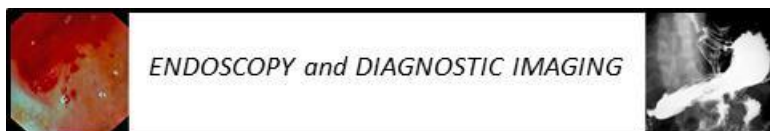


between love and justice, and you place your family and friends at the top of your wish-list of lifetime achievements.

For the skeptics who ask “What do you want from me?” I simply say “You are the future; I trust that in time you too will help young people to be the best they can be.”

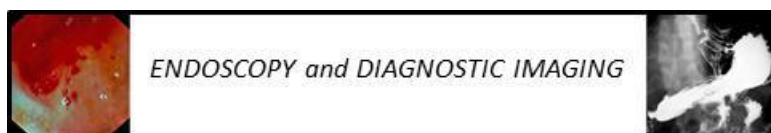
May good luck, good health, modesty, peace, and understanding be with you always. Through medicine, all persons of the world may come to share caring, respect, dignity, and justice.

Sincerely,

A handwritten signature in black ink, reading "Alan Thompson". The signature is written in a cursive, flowing style.

Dedication

We dedicate this book to all gastroenterologists
in training, or starting a gastrointestinal career.



Acknowledgments

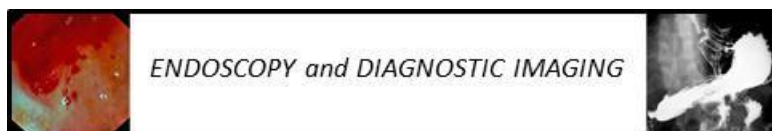
Patience and patients go hand in hand. So also does the interlocking of young and old, love and justice, equality and fairness. No author can have thoughts transformed into words, no teacher can make ideas become behavior and wisdom and art, without those special people who turn our minds to the practical - of getting the job done!

Thank you, Naiyana and Duen, for translating those terrible scribbles, called my handwriting, into the still magical legibility of the electronic age. My most sincere and heartfelt thanks go to the excellent persons at JP Consulting, and CapStone Academic Publishers. Jessica, you are brilliant, dedicated and caring. Thank you.

When Rebecca, Maxwell, Megan Grace, Henry and Felix ask about their Grandad, I will depend on James and Anne, Matthew and Allison, Jessica and Matt, and Benjamin to be understanding and kind. For what I was trying to say and to do was to make my professional life focused on the three C's - competence, caring, and compassion - and to make my very private personal life dedicated to family - to you all.



SKIN, NAIL, and MOUTH CHANGES in GI DISEASE



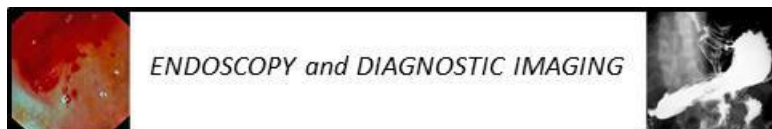
CLINICAL SKILLS

Self-assessment

Extraintestinal changes seen in patients with GI disease.

**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**

Provided through the courtesy of Dr. John McKaigney, University of Alberta



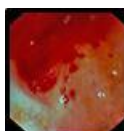
Extra-intestinal changes seen in patients with GI disease

Case 1



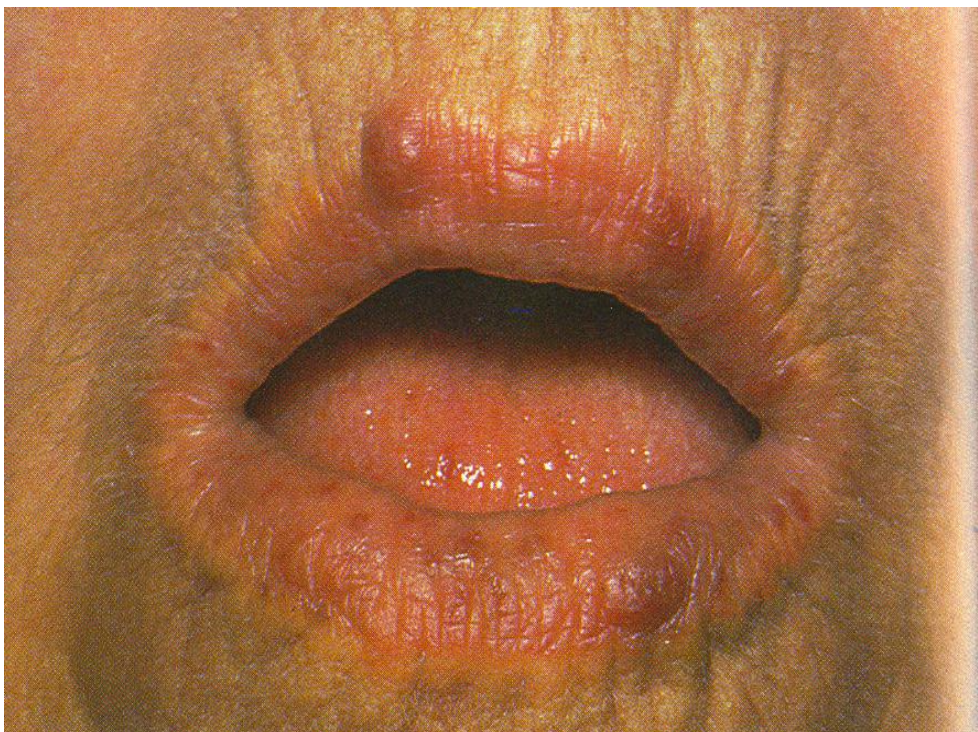
Case 2

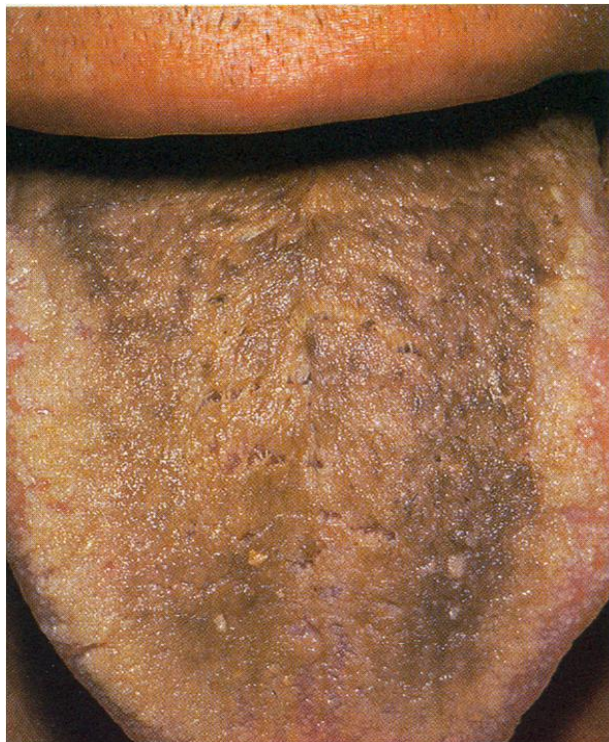
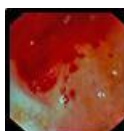
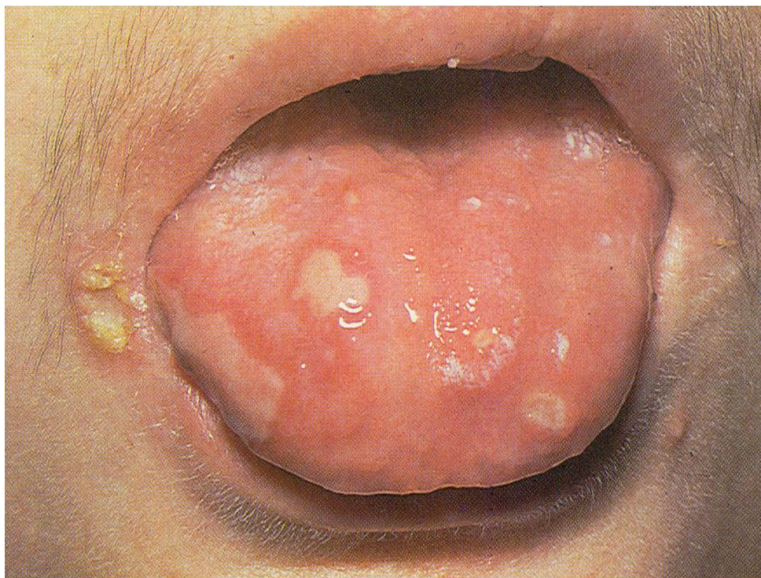
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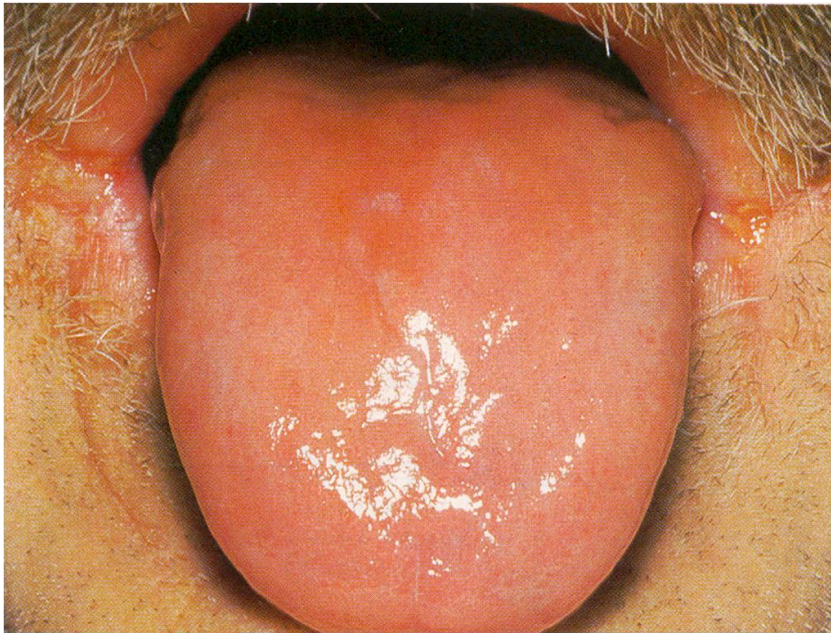
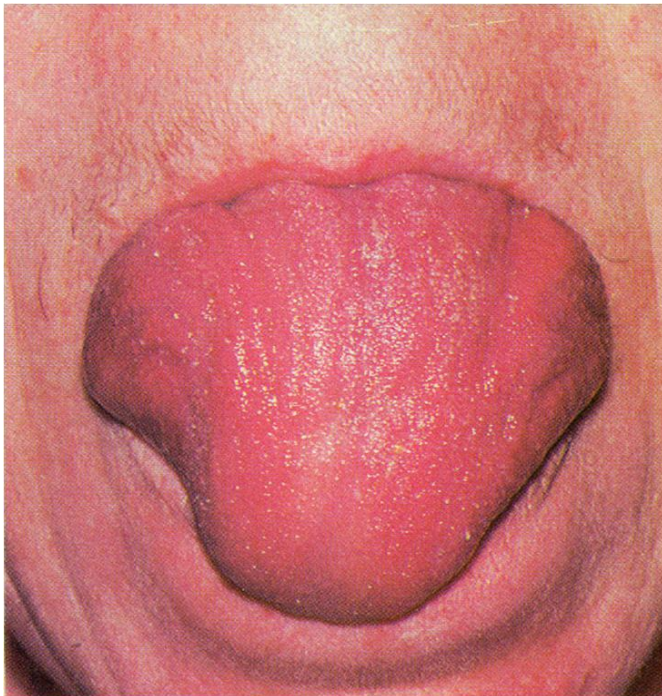


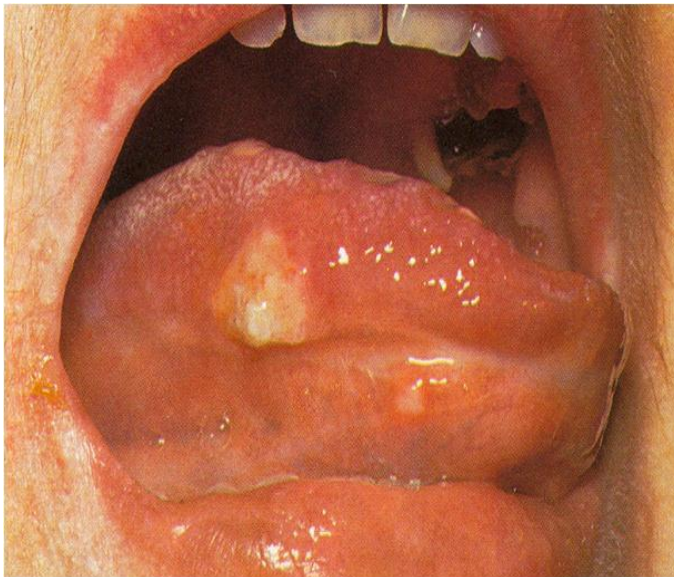
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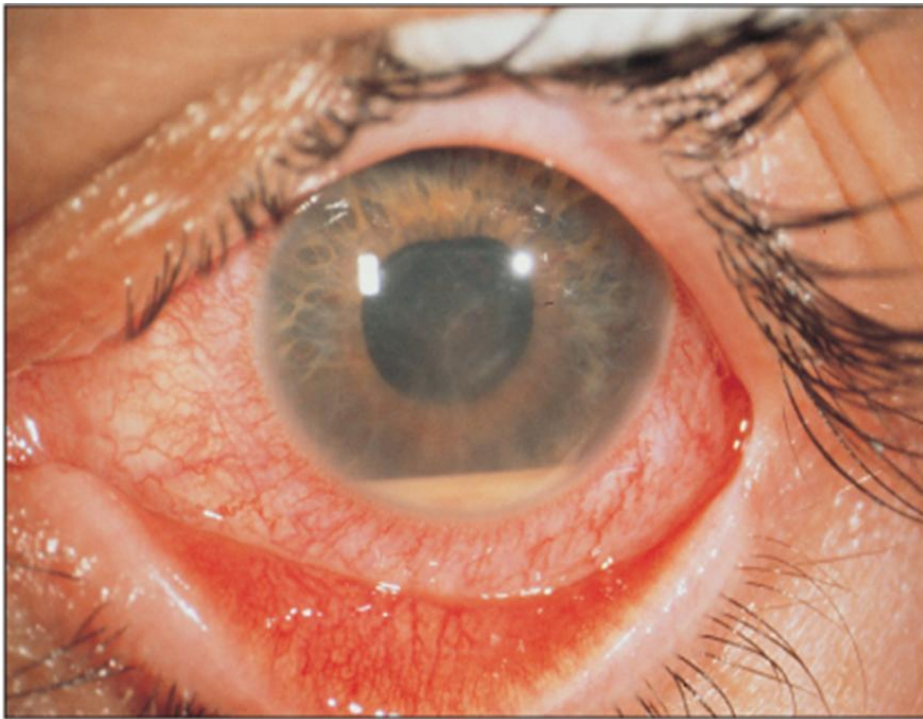


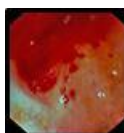
Case 3**Case 4**

Case 5**Case 6**

Case 7**Case 8**

Case 9

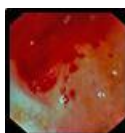
Case 10**Case 11**

Case 12**Case 13**

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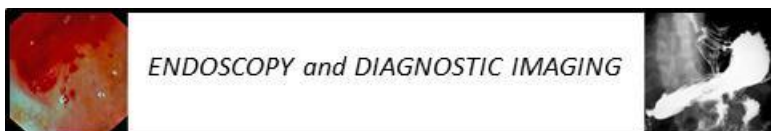
Case 14**Case 15**

Case 16**Case 17**

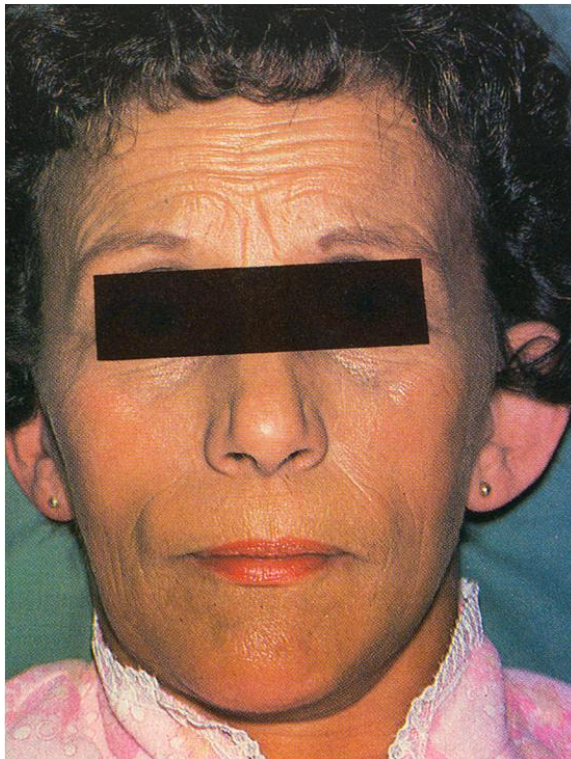
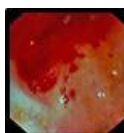
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Case 18**Case 19**

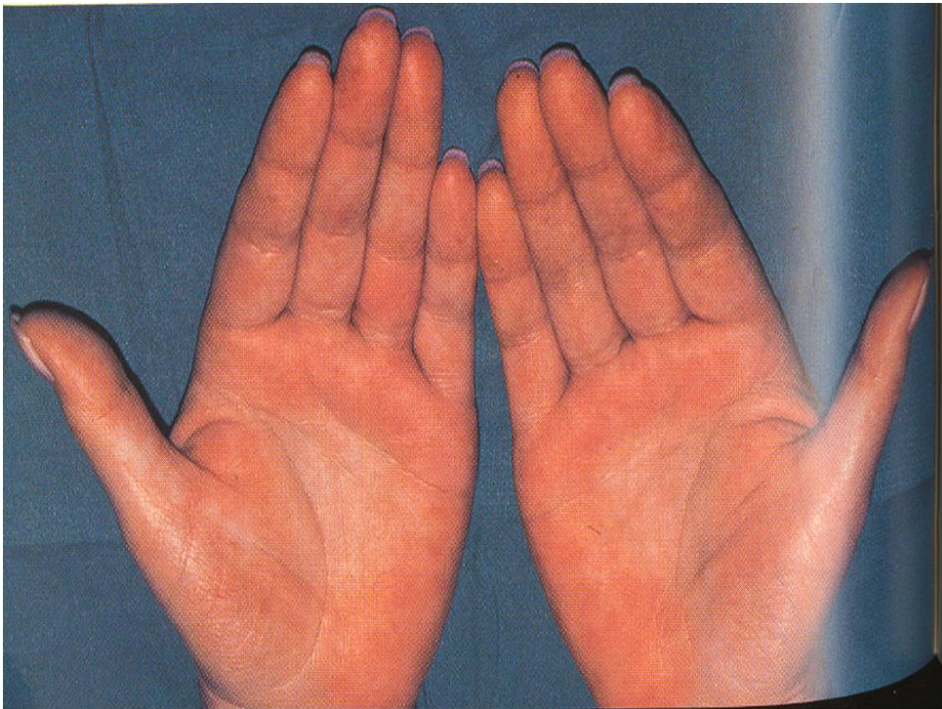
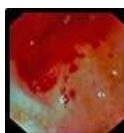
Case 20**Case 21**

Case 22**Case 23**

Case 24**Case 25**

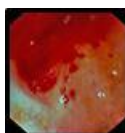
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Case 26**Case 27**

ENDOSCOPY and DIAGNOSTIC IMAGING



Case 28**Case 29**

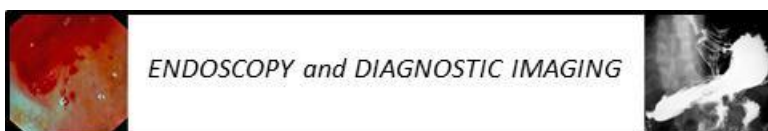
ENDOSCOPY and DIAGNOSTIC IMAGING



Case 30**Case 31****Case 32**

Skin, Nail and Mouth Changes in GI diseases Case Answers

1. Scleroderma
2. Crohn's disease
3. Peutz-Jegher's syndrome
4. Osler weber rendu
5. Black Tongue—Bismuth, Licorice, Fungal infection, Post antibiotic
6. Canker Sores and Angular Cheilosis
7. Glossitis
8. Macroglossia
9. Behcet's syndrome—Oral and genital ulceration
10. Anterior uveitis
11. Xanthelasmata
12. Dermatomyositis
13. Acanthosis nigricans
14. Spider angioma
15. Blue rubber bleb nevus syndrome
16. Leukocytoclastic vasculitis
17. Dermatitis herpetiformis
18. Cullen's sign
19. Grey Turner's sign—Flank hemorrhage—again in acute pancreatitis
20. Erythema nodosum
21. Pyoderma gangrenosus
22. Ascitic abdomen with caput medusa type veins and umbilical hernia
23. Caput medusa
24. Skin pigmentation—hemochromatosis
25. Carotenemia
26. Palmar erythema
27. Dupuytren's
28. White nails
29. Beau's lines
30. Nail pitting-psoriasis
31. Psoriatic Nails
32. Calcinosis crest syndrome



ESOPHAGUS

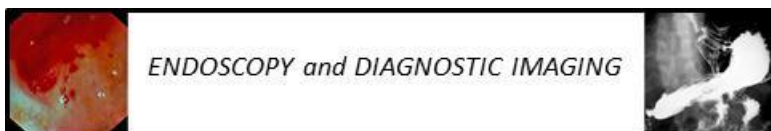
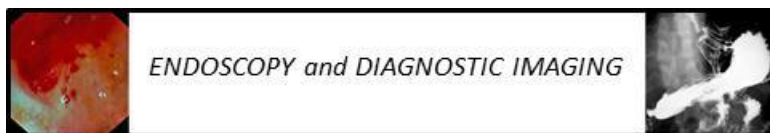


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Standard manometry	83



ESOPHAGUS

“Sharpening Knowledge to Enhance Clinical Skills”

DYSPHAGIA

Practice Pointers: Dysphagia

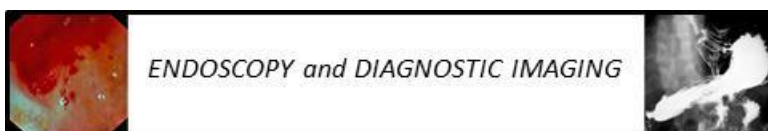
- Pre-esophageal Oropharyngeal Dysphagia
 - Inability to initiate the act of swallowing
 - Tongue fails to push the bolus into the hypopharynx
 - Fluid regurgitates through nose, or tracheal aspiration occurs
- Esophageal Dysphagia
 - Difficulty transporting of ingested material down the esophagus
 - Neuromuscular dysfunction or mechanical physical narrowing (>50% of luminal diameter lost)
- Dilation for Dysphagia:

21 FG (7 mm)	–	liquids only
30 FG (10 mm)	–	pureed food
39 FG (13 mm)	–	soft diet
45 FG (15 mm)	–	regular diet with some limitations (skins etc.)
50 FG (16 mm)	–	regular diet without limitations

(FG = French gauge (circumference) = diameter X pi (3.14))
- Esophageal Bougie Dilation:
 - Overall complication rate 0.1–0.6%
 - Mortality rate 0.05%
 - Perforation 0.5%
 - Guide wire perforation <0.01%
- Grading of Dysphagia:
 - 0 Normal
 - 1 Occasional difficulty with swallowing solids
 - 2 unable to swallow solid food
 - 3 unable to swallow minced food
 - 4 unable to swallow pureed or liquid food
 - 5 unable to swallow liquids or saliva

Practice Pointers:

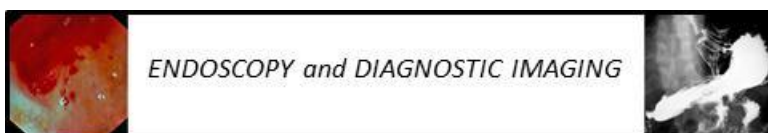
- Benign Stricture
 - Rare in patients with GERD



- Dysphagia occurs when the esophageal lumen becomes narrowed to 12 mm
- Dysphagia with solids, intermittent, slow progression over many months
- No pain except when solids are stuck
- Pre-existing heartburn may decrease or even disappear as dysphagia develops
- Esophagus is heat and alcohol sensitive
- Malignant stricture
 - Dysphagia begins when about half the esophageal circumference is blocked
 - Dysphagia is continuous and progressive; progression is usually rapid
 - Dysphagia first for solids, then for liquids
 - Esophagus not sensitive to heat or ethanol
 - Late pain after mediastinal spread
- Achalasia
 - Slow onset of dysphagia, with slow progression over months
 - Dysphagia equally severe with liquids and solid food
 - There is often concomitant regurgitation together with substernal fullness
 - There is no typical impact pain, and pain may be provoked by eating
 - Spontaneous chest pain is common
 - Altered sphincter tone causing dysphagia can be overcome by pressure from well centered endoscope
- Diffuse Esophageal Spasm
 - Symptoms of dysphagia and/or chest pain (non-cardia chest pain [NCCP])
 - Manometric presence of peristalsis with greater than 30% synchronous waves, waves of amplitude greater than 200 mm Hg, and waves of longer than 7 seconds duration
 - Barium diagnostic imaging may show characteristic “nutcracker” esophageal pattern

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

- A pathophysiological classification of GERD and GERD symptoms, and use this to classify the drugs used to treat persons with GERD.
- Motility disorders
 - Transient lower esophageal relaxations*
 - Esophageal
 - LES



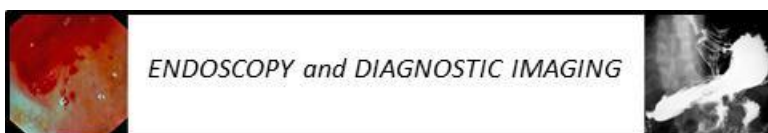
- Cholinergics (bethanecol)
 - Gaba receptor agonists (baclofen)
 - Hiatus hernia
 - Stomach (gastroparesis), obstructive sleep apnea
 - Prokinetics
 - Weak lower esophageal sphincter*
 - Weak esophageal peristalsis
 - Scleroderma and CREST
 - Delayed gastric emptying
- Damaging factors
- Normal /↑ HCl secretion, but ↑ reflux of acid
 - Alginate, antacids, H₂Ras, PPIs
 - Increased gastric acid production
 - Bile and pancreatic juice
 - Sulcrafate
- Resistance factors
- Reduced saliva and HCO₃ production
 - Chewing gum
 - Diminished mucosal blood flow
 - Growth factors, protective mucus
 - Perception
 - TCAs, SSRIs

Abbreviations: GERD, gastroesophageal reflux disease; H2RA, histamine 2 receptor antagonist; LES, lower esophageal sphincter

Printed with permission: Murray JA. *Mayo Clinic Gastroenterology and Hepatology Board Review* 2008: pg. 3.

Practice Pointers: Gastroesophageal Reflux Disease (GERD)

- *“All individuals exposed to the physical complications from gastroesophageal reflux or who experience clinically significant impairment of health related well being (quality of life) due to reflux-related symptomatic esophageal reflux”*
 - Symptomatic GERD (s-GERD), with no endoscopic evidence of esophagitis (normal endoscopy reflux disease [Non-erosive GERD]) but 1/3 to 1/2 have abnormal 24 hr esophageal pH study; Non-erosive GERD patients may have hyperalgesia (increased visceral sensitivity, lessened by atropine)
 - Esophagitis (e-GERD), with risk of ulcer, bleeding, short stricture
 - Barrett esophagus, metaplasia, dysplasia, adenocarcinoma
 - Extra-esophageal reflux complications (eg. ENT, lung)

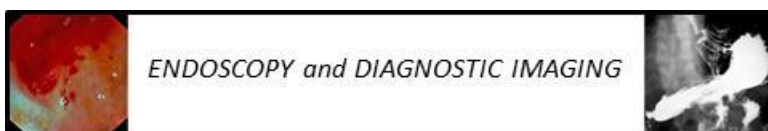


Practice Pointers: GERD: Epithelial Resistance Factors

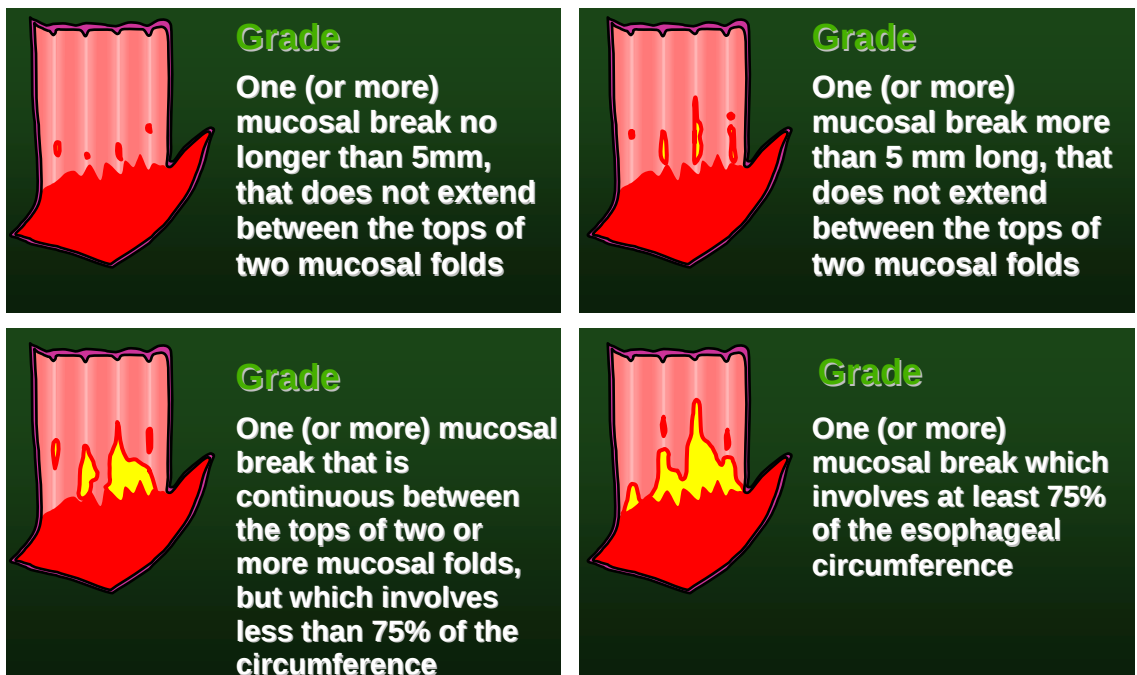
- Pre-epithelial defence
 - Mucus layer
 - Unstirred water layer
 - Surface bicarbonate ion concentration
- Epithelial defence
 - Apical cell membrane
 - Junctional barriers
 - Intracellular and extracellular buffers
 - pH regulatory processes
- Post-epithelial defence
 - Blood flow
 - Tissue acid-base balance

Practice Pointers: Heartburn

- Heartburn: A burning feeling rising from the stomach or lower chest towards the neck
- Acid is central to GERD symptoms:
 - Acid-peptic attack
 - weakens cell junctions
 - leads to a widening of cell gaps
 - Allows increased acid penetration
 - Penetration of acid and pepsin
 - allows contact of acid with nerve endings
 - disrupts intracellular mechanisms leading to cell rupture
 - Further mucosal damage

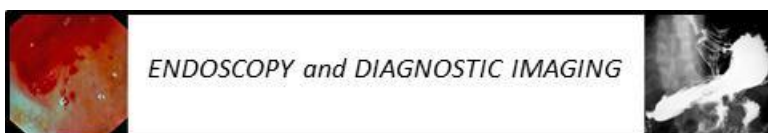


Practice Pointers: The LA Classification system for the endoscopic assessment of reflux esophagitis



Practice Pointers: GERD Endoscopic Grading

- Normal Pattern of esophageal mucosa on high resolution video-endoscopy (with facilities for image processing, and routine use of Lugol's iodine staining)
- Pin-point/Comma Shaped Blood Vessels seen in squamous mucosa above the squamo-columnar junction
- Branching Blood Vessels seen in columnar mucosa below the squamo-columnar junction
- Serrated squamo-columnar junction: Saw tooth incursion into squamous mucosa, with the depth of each saw-tooth greater or equal to its width
 - Definition of Extent of serrations: three or more serrations should be seen per radial gastric fold
- Triangular Indentation into squamous mucosa by villiform columnar mucosa, with or without apical mucosal break
- Palisade Blood Vessels: longitudinal blood vessels not visible in squamous mucosa above the squamo-columnar junction
- Villiform Mucosa: villous-like mucosa immediately below the squamo-columnar junction



Practice Pointers: Esophageal strictures

- Long
 - Peptic ulcer disease
 - NG suction
- Irregular
 - Squamous/adenocarcinoma
- Short-GERD

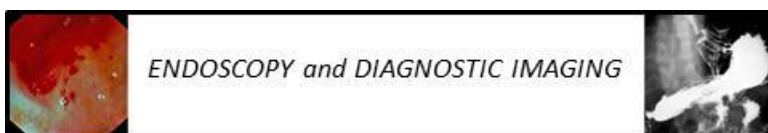
Practice Pointers: Motor Abnormalities after Healing of erosive GERD with acid suppressants

- The motor disorder remains, despite mucosal healing (ie, disorder is primary)
- Continued low
 - Basal LES
 - Body contraction amplitude
 - Esophageal transit (long transit time)

Practice Pointers: Predictors of recurrence in GERD

- Initial severity of mucosal injury
 - Initial severity of reflux symptoms
 - Persistent / residual symptoms during healing phase
 - Slow healing and refractoriness to H2RA
 - Severity of motor disorder and lowering of basal LES pressure
- The non-dietary causes/associations (not pathophysiology) of GERD.
 - Hiatal hernia
 - Scleroderma, Sjögren syndrome
 - Gastroparesis
 - Zollinger-Ellison syndrome, G cell hyperplasia
 - Pregnancy, ascites, obesity
 - Smoking, immobility, NG tube
 - Medications (calcium channel blockers, theophylline, anticholinergics, nitrates, alpha adrenergic antagonists), Botox injections
 - Vagotomy, gastrectomy, post dilation or myotomy for achalasia, bariatric surgery

Abbreviation: GERD, gastroesophageal reflux disease



- The diagnostic tests for GERD

- Tests to assess reflux

- Intraesophageal pH monitoring
- Ambulatory bilirubin monitoring (bile reflux)
- Ambulatory esophageal impedance and pH monitoring
- Barium esophagogram, video fluoroscopy swallowing study (VFSS)
- Scintigraphy

- Tests to assess symptoms

- Empirical trial of acid suppression

		<u>Sensitivity %</u>	<u>Specificity %</u>
- Heartburn and regurgitation	twice daily for 7 days	80	56
- Noncardiac chest pain	twice daily for 14 days	75	85

- Intraesophageal pH monitoring with symptom association analysis
- Bernstein test (acid infusion test to reproduce patient's typical symptoms)
- Corticol sensing and motor control

- Tests to assess esophageal damage

- Endoscopy (optical white light EGD, capsule endoscopy (CE), EUS/FNA narrow band imaging (NBI) with zoom, chromoendoscopy)
- Esophageal biopsy
- Contrast radiography

- Tests to assess esophageal function

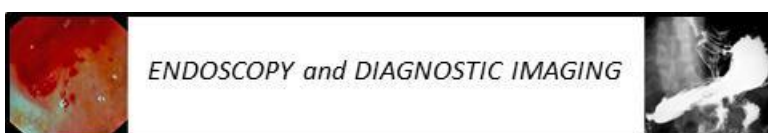
- Esophageal manometry (normal and high resolution)
- Esophageal impedance
- VFSS

Abbreviations: CE, capsule endoscopy; GERD, gastroesophageal reflux disease; FNA, fine needle aspiration; NBI, narrow band imaging

Adapted from: Richter JE. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 916.; printed with permission: Murray JA. *Mayo Clinic Gastroenterology and Hepatology Board Review*: pg. 11.; Thomson ABR. *Clinical Medicine Gastroenterology* 2008;1:pg. 11.; and Spechler SJ. *2008 ACG Annual Postgraduate Course book*: pg. 113.

Practice Pointers: Disadvantages of Surgical Therapy of GERD

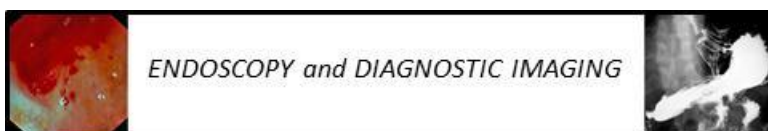
- Highly operator-dependent
- Surgical therapy not standardized



- Unpredictable end result in individual patient!
- Substantial morbidity ~8-10%
- Low but definite mortality!
- (posterior wall perforation) (~0.1-1%)
- Transient dysphagia ~40% (dilatation necessary)
- Permanent dysphagia
- Gas-bloat syndrome
- Abdominal pain
- Vagal damage
- Disappointing results after redo surgery (necessary in ~10%)

Practice Pointers: Esophageal Barrett's epithelium (BE; Intestinal Metaplasia [IM]) in GERD

- Lifetime prevalence ~ 10–16%
- Annual incidence
 - long segment ~ 1%
 - short segment ~ 0.4%
- Composite incidence in adenocarcinoma
 - long segment BE 1 per 125–200 patient/observation years!
- The pathophysiology of GERD, and classify the drugs used to treat this condition.
 - ↓ TLESF – baclofen (gabba receptor agonist)
 - ↑ LESF – bethanecol
 - ↓ sensation – TCA
 - ↓ reflux – alginate
 - ↓ acid – PPI, H₂RA, antacids
 - ↑ gastric emptying – motilium
 - ↑ saliva – chewing gum
- Histological abnormalities in GERD.
 - Reactive epithelial changes
 - Hyperplasia of the basal zone
 - Elongation of papillae
 - Increased mitotic figures
 - Increased vascularization of the epithelium
 - Loss of usual longitudinal orientation of the surface epithelium
 - Balloon cells



- Erosions
 - Epithelial loss
 - Inflammatory infiltrates – lymphocytes, plasma cells, eosinophils, neutrophils
 - Necrosis
- Barrett's
 - Intestinal metaplasia, dysplasia, adenocarcinoma
 - Goblet cells (shown with combined hematoxyline and eosin-alcian blue PAS stains)
 - Fibrosis

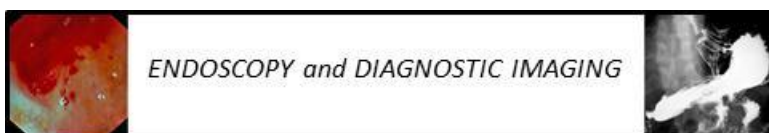
Abbreviation: GERD, gastroesophageal reflux disease

- In a patient in whom Barrett's epithelium (BE) is suspected. Give 4 molecular tests which may suggest the presence of dysplasia.
 - DNA aneuploidy
 - Ki67 (proliferation) – increased expression on immunohistochemistry
 - Oncogenes – cyclin D1, TGF α , EGFR, Ras, B-catenin
 - Tumor suppressors genes
 - Anti-apoptosis genes
 - Anti-senescence markers - telomerase

Printed with permission: Flejou JF. *Best Practice & Research Clinical Gastroenterology* 2008; 22(4): pg. 680.

- The suggested recommendations for endoscopic surveillance of persons with Barrett's Esophagus (BE).
- GERD symptoms > 10yrs, 3 times per week, severe symptoms

“A lot of things in medicine that make sense,
don't work out”

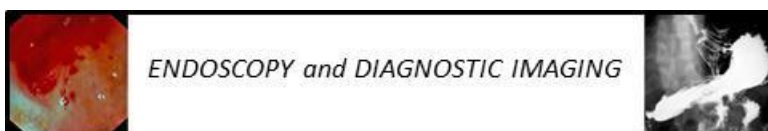


- American College of Gastroenterology recommendations for surveillance by esophageal gastroduodenoscopy (EGD)

Dysplasia	Documentation	Follow-up EGD
○ None (metaplasia)	2 EGDs with biopsy (4 quadrant, q 2 cm), confirm by two expert pathologists	3 - 5 years
○ LGD	Repeat EGD with biopsy, when erosive esophagitis healed, confirm by two expert pathologists, confirm with #3 EGD plus biopsies to exclude HED/EMC	q 1 year until no dysplasia
○ HGD – Focal (<5 crypts)	Repeat EGD with biopsy to rule out cancer/document HGD expert pathologist confirmation	q 3 months
○ HGD – Multifocal (>5 crypts)		Radiofrequency ablation, PDT, endoscopic therapy, esophagectomy in surgical candidate (see question 25, page 31)

Abbreviations: BE, Barrett's epithelium; EGD, esophageal gastroduodenoscopy; EMR, endoscopic mucosal resection; EUS, endoscopic ultrasound; GERD, gastroesophageal reflux disease; HGD, high grade dysplasia; LGD, low grade dysplasia; PDT, photodynamic therapy

- The endoscopic therapies for Barrett's esophagus (BE) with high grade dysplasia (HGD) or early mucosal cancer (EMC).
 - Nd: YAG laser
 - Argon plasma coagulation (APC)
 - Photodynamic therapy (PDT) with porfimer or 5-aminolevulinic acid (5-ALA)
 - Radiofrequency ablation (RF)
 - Cryotherapy
 - Endoscopic mucosal resection (EMR)
 - Esophagectomy in surgical candidate

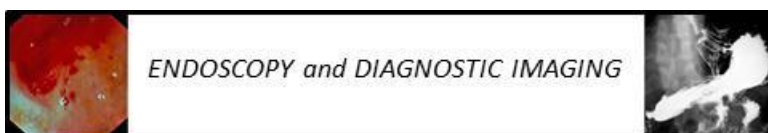


Abbreviations: 5-ALA, 5-aminolevulinic acid; APC, argon plasma coagulation; BE, Barrett's esophagus; EMC, early mucosal cancer; HGD, high grade dysplasia.

Printed with permission: Curvers WL, Kiesslich R, Bergman JJ. *Best Prac Res Clin Gastroenterol* 2008; 22(4):687-720.

Endoscopic changes in Non-erosive GERD

- Normal pattern of GE junction
 - Sharply demarcated squamo-columnar mucosal junction
 - Delicate parallel vascular palisade zone
 - Uniform iodine-staining of glycogen
 - Regular non-interrupted parallel rete or ridge pattern
- High Resolution Endoscopy (Early Lesions of Non-erosive GERD/GERD)
 - Jagged irregular SC mucosal junction
 - Minute triangular defects
 - Disrupted rete-pattern and microscarring
 - Irregular lugol-staining
 - Abnormal vascularisation
 - Villiform appearance below z-line
- **Criterion 1: Pin-point/Comma Shaped Blood Vessels**
 - Pin-point or comma-shaped blood vessels seen in squamous mucosa above the squamo-columnar junction
- **Criterion 2: Branching Blood Vessels**
 - Branching blood vessels seen in columnar mucosa below the squamo-columnar junction
- **Criterion 3: Serrated squamo-columnar junction**
 - Definition of Serration: Saw tooth incursion into squamous mucosa, with the depth of each saw-tooth greater or equal to its width
 - Definition of Extent of serrations: three or more serrations should be seen per radial gastric fold.
- **Criterion 4: Triangular Indentation**
 - Triangular indentation into squamous mucosa by villiform columnar mucosa, with or without apical mucosal break
- **Criterion 5: Palisade Blood Vessels**



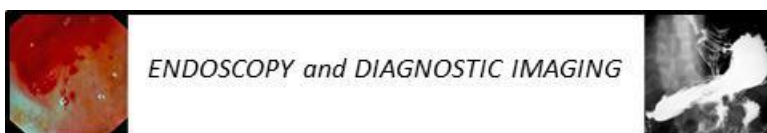
- Longitudinal blood vessels only faintly visible in squamous mucosa above the squamo-columnar junction
- **Criterion 6: Villiform Mucosa**
 - Villous-like mucosa immediately below the squamo-columnar junction

Practice Pointers: How important is non-erosive GERD?

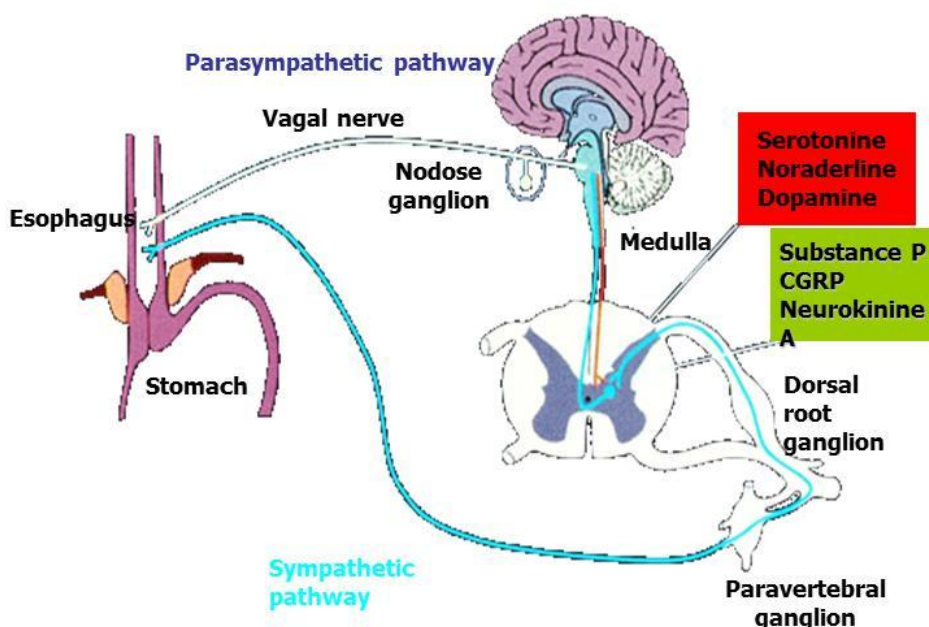
- 60% of all GERD patients in the community have Non-erosive GERD
- Symptoms and QoL impact similar to erosive esophagitis
- Not all Non-erosive GERD patients have abnormal acid exposure! The “tender” esophagus
- Overlap of Non-erosive GERD with functional dysplasia (FD)
- Lifestyle modifications for Gastroesophageal reflux disease, including Non-erosive GERD
 - Tight garments and obesity
 - Foods that decrease LES pressure (Fat, caffeine, chocolate, peppermint, alcohol)
 - Smoking?
 - Drugs (Ca antagonists, nitrates, theophyllines, anticholinergics, beta blockers)
 - Pregnancy
 - Large meals that distend the stomach
 - Recumbency after meals

Practice Pointers: Transient LES relaxations (TLESR)

- Physiological significance:
 - Venting of swallowed air during belching
- Stimuli:
 - Distension of gastric fundus
 - Pharyngeal stimulation
 - CCK Release
- Pharmacological Blockade of TLESRs
 - Atropine
 - Hyoscine n-butyl bromide
 - Loxiglumide / devazepide
 - L-NMMA / L-NAME
 - Baclofen
 - Morphine



Practice Pointers: Visceral Perception in the Esophagus, which may be important in Non-erosive GERD.

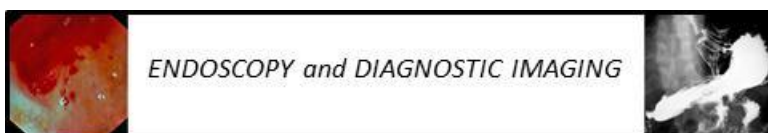


Recent Updates: Non-erosive GERD

- Persons with typical symptoms of gastroesophageal reflux disease (GERD) may have an endoscopically normal mucosa and be diagnosed as having nonerosive reflux disease (Non-erosive GERD). This is sufficient for clinical practice, but in a research setting, Non-erosive GERD may be classified into three groups:
 - Abnormal esophageal acid exposure time (41% of Non-erosive GERD patients)
 - Hypersensitive esophagus: normal esophageal acid exposure, positive symptom associated with acid or non-acid reflux (32% of Non-erosive GERD patients)
 - Functional heartburn: normal esophageal acid exposure; negative symptom association with acid or non-acid reflux (27% of Non-erosive GERD patients)

Useful background: Longterm PPI Therapy

- Peculiarities of Intra-gastric Acidity
 - Effects on gastric pH
 - Nocturnal acid breakthrough
 - Tachyphylaxis?

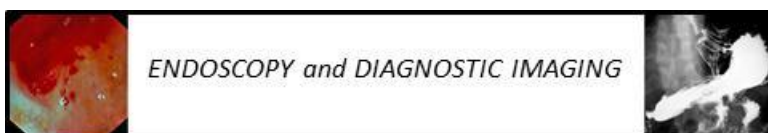


- Rebound?
- Nocturnal Acid Breakthrough (pH<4 for >1 hour)
 - Occurs in up to 70% of GERD patients treated with PPI bid, especially Hp-negative
- Acid Rebound with PPI's
 - Occurs 7 days following cessation of 2–3 months high-dose PPI treatment
 - Increases BAO but more consistently MAO (but an unphysiological stimulus)
 - May last up to 11 months
 - May not be seen in *H. pylori*-positive patients
 - Mechanism uncertain ? Hypergastrinemia ® enterchromaffin cell hyperplasia
 - Relevance to symptom relapse?

Adapted from: Waldum, Gut 1996;39:649-53; Gillen et al, Gastroenterology 2001(A); Gillen et al, Gastroenterology 1999;116:239-47

- Altered metabolism of alcohol
 - Bacterial overgrowth particularly aërobes causes acetaldehyde production from alcohol-acetaldehyde is a local carcinogen
 - Poor acetaldehyde metabolizers due to mutant ALDH2 have 2–3 times higher in vivo salivary acetaldehyde levels after moderate amounts of alcohol (oriental flushers)
- Morphologic Changes in Gastric Mucosa in persons on longterm PPIs
 - Expansion ECL mass
 - Expansion parietal cell mass
 - Parietal cell protrusions
 - Fundic gland polyps
 - ? Acceleration of atrophy in *H.p.*- positive
- Increased Risk of Enteral Infection?
 - One case of bacterial diarrhea per 3,319 PPI prescriptions
 - PPI therapy may be a risk factor for campylobacter enteritis (Odds ratio 11.7)

Adapted from: Nwokolo, Eur J Gastro Hep 1994;6:697; Neal, BMJ 1996;312:414

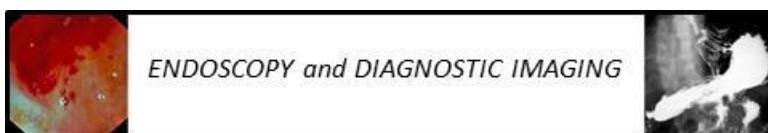


- Bacterial Overgrowth
 - Most obvious in Hp-positive
 - High nitrite levels
 - Low ascorbic acid levels → more N-nitroso compounds

Adapted from: Mowatt, Gastroenterology 2000;119;339

- **The potential risks of long-term PPI therapy.**

	Risk magnitude/possible consequence
➤ Hypergastrinemia-induced carcinoid tumors	Not demonstrated in humans
➤ Accelerated progression of atrophic gastritis/gastric cancer with concomitant <i>H. pylori</i> gastritis	No documentation of an increase in atrophic gastritis and no basis to recommend testing or treatment for <i>H Pylori</i> before long-term PP use
➤ Formation of gastric fundic gland polyps	Odds ratio of 2.2 for developing Fundic gland polyps within 1-5 years, negligible, if any, risk of dysplasia
➤ Vitamin B ₁₂ malabsorption	Some patients show decreased vitamin B ₁₂ levels after years of acid inhibition, case reports (2) of clear deficiency
➤ Calcium malabsorption	Nested case-control study of UK patients older than 50 years; adjusted odds ration of 1.44 (95% confidence interval, 1.30-1.59) of hip fracture with PPI use longer than 1 year
➤ Iron malabsorption	Poor response to oral iron supplement absorption in 2 iron-deficient individuals improved after cessation of Omeprazole; no clear clinical relevance
➤ Increased risk of <i>C difficile</i> colitis	PPI use is independent risk of <i>C difficile</i> diarrhea in antibiotic users, odds ratio of 2.1 (95% confidence



interval, 1.2-3.5)

- Increased risk of community-acquired pneumonia (presumably aspiration)
 - Nested case-control analysis, adjusted odds ratio for pneumonia with PPI use of 1.73 (95% confidence interval, 1.33-2.25)

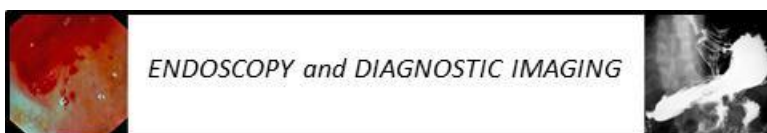
Risk magnitude/possible consequence

-
- | | |
|--|---|
| ➤ Gastric colonization with bacteria that convert nitrates to carcinogenic <i>N</i> -nitroso compounds that then reflux | Data on PPI use and increased gastric <i>N</i> -nitrosamine remain uncertain and the risk of cancer is speculative |
| ➤ Safety in pregnancy (Omeprazole crosses placenta and is pregnancy safety category C; other PPIs are category B) | Based on 345 accidental exposures compared with 787 controls, no observed increased teratogenicity |
| ➤ Drug-drug interactions; PPIs metabolized by cytochrome P450 and may induce or inhibit drug metabolism (phenytoin, warfarin, Plavix®) | Clinically significant PPI drug-drug interactions are rare (<1/million prescriptions) |
| ➤ Anaphylaxis | One case report with lansoprazole |
| ➤ Acute interstitial nephritis | 64 cases worldwide, partially reversible (one case requires dialysis, no deaths), estimated risk 1/12,500 patient-years of therapy) |
| ➤ Pancreatitis | Population-based case-control study adjusted odds ration of 3.2 (95% confidence interval, 1.4-7.4) |

Printed with permission: AGA Technical Review. *GE* 2008;135: pg. 1392-1413.

- **The etiologies of benign, non-GERD related esophageal strictures.**

- Congenital—strictures, atresia
- Drugs and chemicals—radiation, caustic, chemical, thermal, quinidine gluconate
- Webs, rings
- Sclerotherapy



- Acid and non-acid causes of esophagitis (see question 13, page 22)
- Surgery--complicated reflux strictures (NG tube, ZE syndrome), ischemia, anastomotic (staples)
- Latrogenic - EMR for BE, prolonged NG tube, therapy, PDT

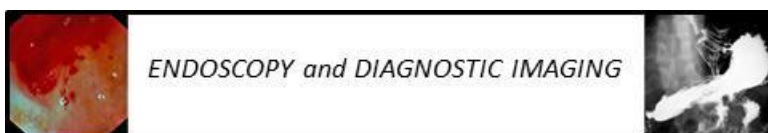
Abbreviations: BE, Barrett's epithelium; EMR, endoscopic mucosal resection; NG, nasogastric tube; PDT, photodynamic therapy; ZE, Zollinger-Ellison syndrome

- The predictors of initial therapeutic failure of pneumatic dilation of benign esophageal strictures (e.g. repeated dilations required).
 - Related to patient
 - Younger age (<40 years)
 - Male sex
 - Wide esophagus
 - Related to procedure
 - Inadequate dilation
 - Small size balloon (30 mm)
 - LES pressure >10 mm Hg post-treatment
 - Poor esophageal emptying post-treatment

Abbreviation: LES, lower esophageal sphincter

Adapted from: Boeckxstaens GEE. *Best Practice & Research Clinical Gastroenterology* 2007;21(4): pg. 595.

- The late risks/complications of laparoscopic Nissen fundoplication.
 - Symptom recurrence
 - Recurrent, persistent GERD symptoms
 - Repeat use of acid-lowering therapy (recidivism, 50% in 5 years)
 - Repeat reflux surgery
 - Surgical problems
 - Wrap too loose – herniation (recurrent hiatus hernia); paraesophageal hernia through an intact fundoplication
 - Slipped fundoplication with recurrent sliding hiatus hernia
 - Wrap too tight – dysphagia – early, 20%; late, 6% (including gas-bloat syndrome requiring dilation, 4%)
 - Diarrhea (vagotomy)
 - Death (0.2-0.8%)



ESOPHAGEAL MOTILITY DISORDERS

- Classify esophageal motor abnormalities, and give the qualitative changes in motility in the UES, EB and LES of 4 conventional manometric (dysmotility) syndromes.

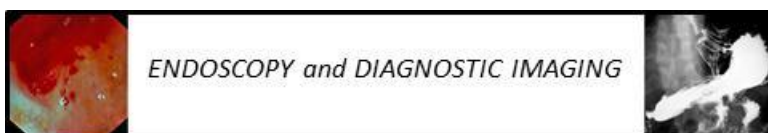
Upper esophageal sphincter (UES)	Esophageal body (EB)	Lower esophageal sphincter (LES)
↑ Contraction ○ Zenker's diverticulum	↑ Contraction ○ Nutcracker esophagus ○ Achalasia (compartmentalized pressurization)	↑ Pressure ○ Isolated hypertensive LES ○ Achalasia
↓ Contraction ○ MCTD (e.g. scleroderma) ○ Oculopharyngeal dystrophy	↓ Contraction* ○ Ineffective esophageal motility (IEM) ○ Aperistalsis (e.g. scleroderma)	↓ Pressure ○ Hypotensive LES ○ GERD (↑ tLESR) ○ Scleroderma
Upper esophageal sphincter (UES)	Esophageal body (EB)	Lower esophageal sphincter (LES)
↓ Co-ordination ○ Achalasia (complicated) ○ Parkinson's disease ○ Cricopharyngeal bar ○ Belch dysfunction	↓ Co-ordination ○ Diffuse esophageal spasm (DES) ○ Achalasia (absent or simultaneous contractions)	↓ Co-ordination ○ (relaxation**) ○ Achalasia, type I ○ Atypical LES relaxation (pseudo-achalasia) ○ Post-fundoplication gas-bloat syndrome

contraction, or impaired retrograde inhibition

** relaxation, or inadequate swallow-induced inhibition

Abbreviations: EB, esophageal body; IEM, ineffective esophageal motility; LES, lower esophageal sphincter; UES, upper esophageal sphincter

Useful background:



- Normal: Normal velocity, <8 cm/s in $> 90\%$ of swallows; normal peristaltic amplitude; (≥ 7 peristaltic contractions with an intact wave progression [amplitude >30 mm Hg])
- Aperistalsis: Absent or simultaneous contractions (<30 mm Hg)
- Ineffective esophageal motility (IEM): ≥ 3 peristaltic contractions with failure of wave progression due to an ineffective distal contraction amplitude (>30 mm Hg) or failed peristalsis over a segment of the distal esophagus
- Nutcracker esophagus: average peristaltic amplitude >180 mm Hg over pressure sensors 3 and 8 cm above LES
- Distal esophageal spasm (DES): contractile velocity >8 cm/s mm Hg over pressure sensors 3 and 8 cm above LES in ≥ 2 swallows
- Isolated hypertensive LES: basal LES pressure greater than 45 mm Hg (mid-respiratory pressure)
- Achalasia: abnormal LES relaxation; absent or simultaneous contractions
- Atypical disorders of LES relaxation: abnormal LES relaxation, with some normal, may have simultaneous or absent peristalsis.

Abbreviations: LES, lower esophageal phincter; TLESR, transient lower esophageal sphincter relaxation; MCTD, mixed connective tissue diseases.

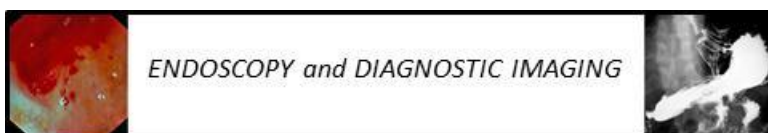
Adapted from: Pandolfino et al. *AJP* 2008;103: pp 28.; and printed with permission: Sifrim D and Fornari F. *Best Practice & Research Clinical Gastroenterology* 2007;21(4): pg. 575-576.

- The advantages of high resolution esophageal manometry, high resolution esophageal pressure topography (HREPT) include:
 - High quality, uniform format, simultaneous contractions of the entire esophagus
 - Standardized objective metrics
 - Topographic patterns easily learned and recognized, with greater reproducibility

Abbreviation: HREPT, high resolution esophageal pressure topography

Useful background: Clinical diagnosis of achalasia

- | | |
|---|---|
| <ul style="list-style-type: none"> ➤ Radiographic <ul style="list-style-type: none"> ○ Esophageal dilatation ○ Poor esophageal emptying | <ul style="list-style-type: none"> ➤ Manometric <ul style="list-style-type: none"> ○ Impaired deglutitive relaxation |
|---|---|



- Bird-beak deformity of LES
- Absent gastric air bubble
- Absent peristalsis (but can have spasm or pressurization)
- Increased LES pressure
- Increased esophageal pressure

Abbreviation: LES, lower esophageal sphincter

Useful background: Chicago classification diagnostic criteria.

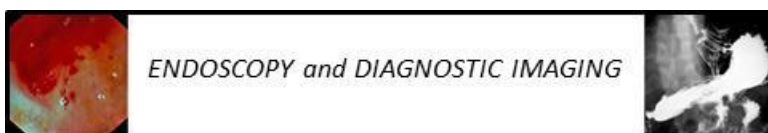
- Distal segment, impaired EGJ relaxation
 - Achalasia
 - Classic achalasia
 - Achalasia with esophageal compression
 - $\geq 20\%$ test swallows with esophageal compression

Printed with permission: Pandolfino JE, et al. *Gastroenterology* 2008;135:1526.

- The treatment response rates of achalasia treatments categorized by pressure topography subtype

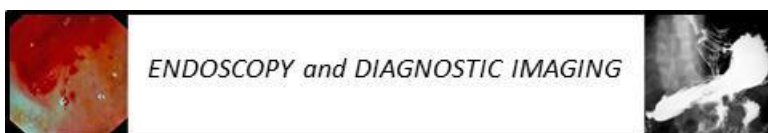
➤ Achalasia subtype First Intervention	Type I Classic	Type II, with compression	Type III spastic	All types
○ Botulinum toxin	0% (0/2)	86% (6/7)	22% (2/9)	39% (7/18)
○ Pneumatic dilation	38% (3/8)	73% (19/26)	0% (0/11)	53% (24/45)
○ Heller Myotomy	67% (4/6)	100% (13/13)	0% (0/1)	85% (17/20)
○ All (any) interventions	44% (7/16)	83% (38/46)	9% (2/21)	56% (47/83)
➤ <i>Subsequent interventions</i>				
○ Number of interventions	1.6 $\pm$ 1.5	1.2 $\pm$ 0.4	2.4 $\pm$ 1.0	1.8 $\pm$ 0.7
○ Successful last intervention	56%	96%	29%	71%
○ Last intervention type	B-O, P-10, M-6	B-6, M-25, M-15	B-8, P-8, M-5	B-14, P-43, M-26

Printed with permission: Pandolfino JE et al. *Gastroenterology* 2008;135:1526.



- The causes of secondary (pseudoachalasia) achalasia.
 - Infection/Infiltration
 - Sarcoidosis
 - Sjogren's syndrome
 - Amyloidosis
 - Fabry's disease
 - Chagas disease (*Trypanosoma cruzi*)
 - Cancer (GI)
 - Squamous cell carcinoma of the esophagus
 - Adenocarcinoma of the esophagus
 - Hepatocellular carcinoma
 - Pancreatic adenocarcinoma
 - Cancer (Non-GI) (Paraneoplastic syndrome)
 - Lung carcinoma (non-small cell)
 - Metastatic prostate carcinoma
 - Metastatic renal cell carcinoma
 - Breast adenocarcinoma
 - Leiomyoma
 - Lymphoma
 - Reticular cell sarcoma
 - Lymphangioma
 - Mesothelioma
 - Motility
 - Parkinson's disease
 - Achalasia with associated Hirschsprung's disease
 - Hereditary hollow visceral myopathy
 - Familial achalasia
 - Surgical
 - Post-fundoplication
 - Post-vagotomy
 - Miscellaneous
 - Allgrove's syndrome (AAA syndrome) – (Alaciditygia; Addisons; Achalesia)
 - Hereditary cerebellar ataxia
 - Autoimmune polyglandular syndrome type II
 - MEN IIb (Sipple's Syndrome)

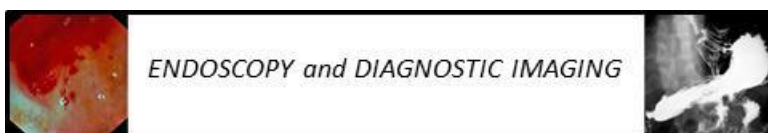
Adapted from: Clouse RE, and Diamant NE. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006:871.



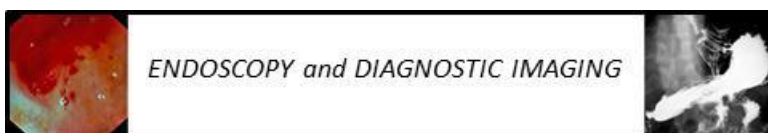
Useful background: Primary treatments for idiopathic achalasia under the headings: response (early, late) morbidity (minor, major).

Comparative Feature	Smooth Muscle Relaxants	Botulinum Toxin Injection	Pneumatic Dilation	Open Surgical Myotomy	Laparoscopic Myotomy
° RESPONSE					
Early	° 50%-70%	° 90% at 1 mo	° 60%-90% at 1 yr	° >90% at 1 yr	° >90% at 1 yr
Late	° <50% at 1 yr	° 60% at 1 yr	° 60% at 5 yrs	° 75% at 20 yrs	° 85% at 5 yrs
° MORBIDITY					
Minor	° 30% (headache, hypotension)	° 20% (rash, transient chest pain)	° Rare technique-related complications	° <10% at 1 yr (symptomatic reflux)	° 10% (symptomatic reflux)
Major	° Not Reported	° Not Reported	° 3%-5% (perforation)	° 10% dysphagia ° <2% mortality	° Not Reported
° ADVANTAGE					
	° Rapidly initiated, well accepted	° Low morbidity, modest response durability, well accepted	° Good response durability	° Best response rate and durability	° Avoids thoracotomy, result is likely equivalent to open technique
° DISADVANTAGE					
	° Inconvenient side effects, tachyphylaxis; poor effect on esophageal emptying	° Repeat injection often required within 1 yr ° Fibroinflammatory reaction at LES	° See Morbidity	° Thoracotomy required severe reflux may develop	° Long-term outcome remains unknown, conversion to open procedure in very small percentage
	° Schelesinger				
	° Fordtran				

Adapted from: Clouse RE, and Diamant NE. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006:pg. 879.



- The diagnostic criteria for esophageal motility abnormalities based on high-resolution manometry.
 - Normal
 - Normal EGJ pressure (10-35 mm Hg) and relaxation (see below)
 - Peristaltic velocity <8 cm/s in >90% of swallows
 - Normal elevation of intra-bolus pressure at <8 cm/s to <30 mm Hg in > 90% of swallows
 - Mean distal contractile index (DCI) <5000 mm Hg·s·cm**
 - Peristaltic dysfunction
 - Mild: 3-6 swallows with failed peristalsis or a >2 cm defect in the 30 mm Hg isobaric contour of the distal esophageal peristalsis (15 mm Hg in proximal-mid esophagus)
 - Severe: ≥ 7 swallows with either failed peristalsis or a >2 cm defect in the 30 mm Hg isobaric contour of distal esophageal peristalsis (15 mm Hg in proximal-mid esophagus)
 - Aperistalsis: Contractile pressure <30 mm Hg throughout mid-distal esophagus in all swallows (*Scleroderma* pattern: aperistalsis with LES pressure <10 mm Hg)
 - Hypertensive dysfunction
 - Peristaltic velocity <8 cm/s in >80% of swallows
 - Mean distal contractile index (DCI) >5000 mm Hg·s·cm**
 - *Hypertensive peristalsis*: mean DCI >5000-8000 mm Hg·s·cm
 - *Segmental hypertensive peristalsis*: hypertensive contraction restricted to mid- or distal esophagus or LOS after-contraction: mean DCI 5000-8000 mm Hg·s·cm
 - Hypertensive peristalsis $\pm$ repetitive or prolonged contraction: DCI >8000 mm Hg·s·cm
 - Esophageal spasm (rapidly propagated contractile wavefront)
 - Peristaltic velocity >8cm/s in $\geq 20\%$ of swallows $\pm$ raised DCI
 - *Diffuse esophageal spasm*: rapid contractile wavefront throughout the distal esophagus
 - *Segmental esophageal spasm*: rapid contractile wavefront limited to mid or distal esophageal segment
 - Rapid elevation of intra-bolus pressure (increased resistance to flow due to functional or structural obstruction in the esophagus or at the esophago-gastric junction [e.g. stricture, post-fundoplication, eosinophilic esophagitis, poorly coordinated contractions])
 - Rapid elevation of intra-bolus pressure to >15 mm Hg in >8 cm/s in $\geq 20\%$ of swallows



- Mild: Intra-esophageal bolus pressure (15 to 30 mm Hg) with $\geq 80\%$ preserved peristalsis
- Severe: Intra-esophageal bolus pressure (>30 mm Hg) with $\geq 20\%$ failed peristalsis

➤ Achalasia

- Impaired deglutative EGJ relaxation and/or opening
- Elevation of intra-esophageal bolus pressure due to resistance to flow at EGJ
 - *Classic*: aperistalsis with no identifiable contractile activity
 - *Vigorous*: with persistent contractile activity (spasm) or gross elevation of intra-esophageal bolus pressure with or without esophageal shortening
 - *Variant*: with preserved peristalsis in the distal esophagus in $\geq 20\%$ swallows

➤ Abnormal LES tone

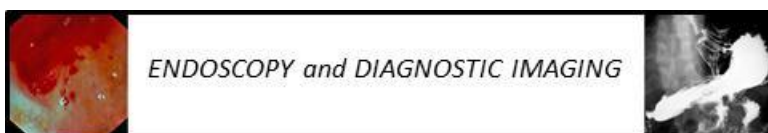
- Hypotensive: 10 s mean <10 mm Hg, with normal peristaltic function
- Hypertensive: 10 s mean >35 mm Hg, with normal peristaltic function and EGJ relaxation

Abbreviations: DCI, distal contractile index; EGJ, esophagogastric junction; LES, lower esophageal sphincter

Printed with permission: Fox MR, and Bredenoord AJ. *GUT* 2008;57: pg. 419.

Useful background:

- One peristaltic contraction rules out achalasia (Katz 09). The motility changes of achlasia include
 - $\uparrow$ LGS pressure
 - $\uparrow$ residual pressure of LGS (incomplete relaxation)
 - Complete absence of peristalsis
- In DES (distal or diffuse esophageal spasm), there is an incertain relationship between symptoms and the DES motility changes
- The nutcracker esophagus and a hypertensive LES may be seen in persons with GERD
- A video barium examination may be normal even when UES manometry is abnormal



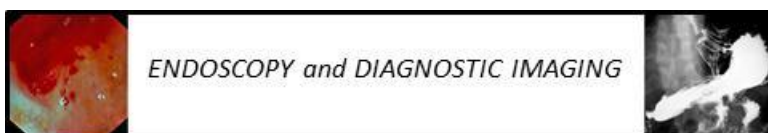
- It is useful to perform provocative testing (intraesophageal acid infusion, balloon distention, edrophonium injection) to attempt to reproduce the patient's symptoms in the setting of NCCP (non cardiac chest pain)
- Combined multichannel intraluminal impedance (MII) and pH testing detects impedance data at 3, 5, 7, 9 and 15 and 17 cm above the LES, and 5 cm above the LES

Abbreviations: DES, distal or diffuse esophageal spasm; DSRS, distal splenorenal shunt; EHT, endoscopic hemostatic therapy; MII, multichannel intraluminal impedance; TIPS, transjugular intrahepatic postoperative shunt

Endoscopic and diagnostic imaging

- Luminal narrowing
 - Long strictures
 - Short webs/rings
 - Filling defects
 - Diverticula/ hernia
 - Perforation
- Long (strictures) mechanical abnormality
 - Foreign body / food bolus
 - Motor abnormality
- Cause of long luminal narrowing
- Mechanical abnormalities (strictures)
 - Peptic
 - Barrett
 - Caustic
 - Radiation
 - Carcinoma
 - Lymphoma (extrinsic compression from lymphadenopathy)
- Food bolus / foreign body
- Motor abnormalities
 - Corkscrew (DES)
 - Achalasia
 - Pseudoachalasia
 - Scleroderma

Abbreviation: DES, diffuse esophageal spasm

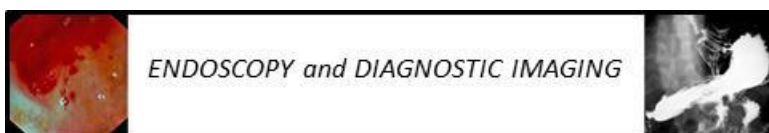


- Cause of short luminal narrowing
 - Upper
 - Cricopharyngeal bar
 - Aberrant right subclavian artery
 - Middle
 - Web
 - Eosinophilic esophagitis
 - Lower
 - Schatzki ring (A,B or C)
- The diseases/conditions associated with a higher risk for sedation-related complications in persons undergoing upper gastrointestinal endoscopy.
 - Morbid obesity
 - Short neck
 - Alcohol or substance abuse
 - Persons on high doses of psychotropic medications
 - COPD, asthma
 - Cervical neck lesions
 - Chronic liver/kidney/heart disease
- The indications for open or laparoscopic surgical fundoplication in the patient with GERD.
 - GERD symptoms responding to PPI, (penalty for failure of PPI as an indication)
 - Intolerance to PPIs
 - Cost of PPIs
 - Patient preference, desire for a “cure”
 - Persistent volume regurgitation
 - Large symptomatic hiatus hernia
 - Respiratory complications from recurrent aspiration
 - Recurrent peptic strictures in a young person

Abbreviations: GERD, gastroesophageal reflux disease; PPI, proton pump inhibitor

Eosinophilic GI disorders

- The causes/associations of eosinophilic gastrointestinal diseases (EGIDs).



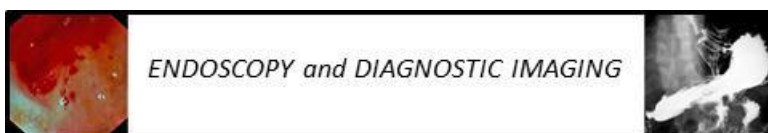
- Idiopathic
 - Eosinophilic syndromes
- Infection
 - Fungal, parasitic and non-parasitic
- Inflammation
 - GSE
 - IBD
 - MC
 - GERD
- Infiltration
 - Neoplasia-associated (e.g. Hodgkin's lymphoma, esophageal leiomyomatosis)
- Immune
 - Autoimmune
 - GVH disease
 - Connective tissue disease (e.g. scleroderma)
 - Hypersensitivity
 - Allergy (e.g. foods)
 - Allergic vasculitis
 - Post-transplant
- Latrogenic
 - Drugs (e.g. gold, azathioprine)

Abbreviations: EGID, eosinophilic gastrointestinal diseases; GERD, gastroesophageal reflux disease; GSE, gluten-sensitive enteropathy; GVH, graft-versus-host disease; IBD, inflammatory bowel disease; MC, microscopic colitis

Adapted from: Mueller S. *Best Practice & Research Clinical Gastroenterology* 2008;22(3): pg. 427.; and Atkins D, et al. *Nat Rev Gastroenterol Hepatol* 2009;6(5): 267-278.

- Classification with respect to blood eosinophilia

Classification	Clinical Features		
	Asthma Allergy	Response to corticosteroids	Recurrence
➤ Group I: with blood eosinophilia	Common	Curative	Common
➤ Group II: without blood eosinophilia	None	No effect	Unknown following removal



- The changes seen on EGD in the patient with eosinophilic esophagitis (EE).

- Corrugation (multiple rings)
- Longitudinal furrows
- Mucosa: featureless, fragile (crepe paper)
- White surface vesicles (eosin microabscess)
- Proximal or mid-esophageal stenosis/stricture
- Small caliber esophagus
- Food impaction

Abbreviations: EE, eosinophilic esophagitis; EGD, esophagogastroduodenoscopy

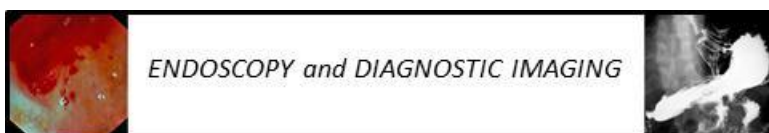
- The complications of eosinophilic esophagitis is a high risk disease

- Dysphagia
- Food impaction
- Stricture
- Sloughing of mucosa (mucosal eosinophils)
- Mucosal tear
- Perforation
 - EGD
 - Spontaneous (Boerhave syndrome) (transmural inflammation)

Abbreviation: EGD, esophagogastroduodenoscopy

- The treatment modalities for eosinophilic esophagitis (EE).

- Educate the patient about diet
 - Elimination diets (milk, soy, eggs, wheat, nuts, seafood)
- Endoscopy
 - Careful esophageal dilation after treatment by diet/drugs
- Drugs
 - Proton pump inhibitor (PPI) bid for 4-8 weeks (poor response)
 - Topical corticosteroids–Fluticasone 220 mcg/puff, 4 puffs BID for 6 weeks; viscous budesonide
 - Leukotriene inhibitors(D₄ receptor antagonist; Singulair®: montelukast)
 - Mast cell stabilizers
 - Anti-IL5 (mepolixumab)
- Surgery

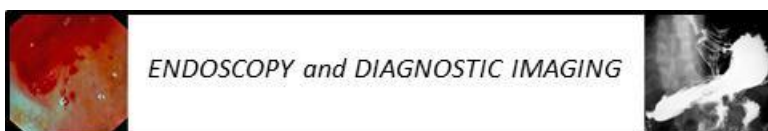


- Try to avoid surgical oversewing (wall does not hold sutures)
- Esophagectomy

Abbreviations: BID, twice a day; EE, eosinophilic esophagitis; PPI, proton pump inhibitor

Diagnostic imaging

- Mucosal irregularity – esophagitis
 - GERD
 - LA A-D
 - Barrett esophagus
 - Drugs and chemicals
 - Infections
 - Candidiasis
 - CMV
 - HSV
 - HIV
- GERD
 - Thick (> 2 mm), nodular folds
 - Erosion – linear / punctuate, superficial
 - Length of esophagus shortened luminal wall irregular narrowed lumen a symmetric sacculations
 - May be hiatus hernia
 - Spiculations buckling of mucosa (from transverse folds from P scar formation following healing of prior linear ulcer)
 - May be ulcerated (LA-D)
 - Ulcer – long, halo of edema
- Barrett esophagus
 - Mucosal erosions
 - Mucosal reticularity
 - Nodularity
 - Granularity
 - Reticular mucosa often near a stricture
- Candida esophagitis
 - Multiple, plaque-like filling defects
 - Anywhere in esophagus
 - May involve entire esophagus
- HSV esophagitis
 - Multiple, small discrete, superficial ulcers
 - Anywhere in esophagus
 - Plaque-like filling defects, multiple
- Giant esophageal ulcers

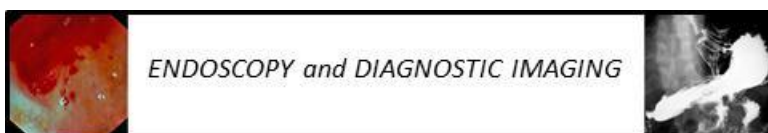


- CMV
- HIV
- CMV esophagitis
 - Large
 - Single, discrete ulcers
 - May not be distinguish able from HSV or HIV esophagitis
- Medication – induced esophagitis
 - Linear, irregular ulcer
 - Surrounding soft tissue mass
 - Localized
 - Usually at aortic arch or distal esophagus
 - Single/ multiple
 - Thickened folds
- Crohn's esophagitis
 - Deep ulceration
 - Confluent ulcers
 - Non-circumferential
 - Aphthous ulcer
 - Small
 - Surrounding halo of edema
 - Fistula
 - Perforation
 - Stricture

ESOPHAGEAL TUMORS

- A classification of benign and malignant esophageal epithelial and non-epithelial tumors.

Epithelial Tumors	Nonepithelial Tumors
➤ Malignant ○ Squamous cell ○ Adenocarcinoma of the esophagus and esophagogastric junction ○ Verrucous carcinoma ○ Carcinosarcoma ○ Small cell carcinoma ○ Malignant melanoma ➤ Benign	➤ Malignant ○ Lymphoma ○ Sarcoma ○ Gastrointestinal stromal tumor (GIST) ○ Metastatic carcinoma ➤ Benign ○ Leiomyoma (50%) ○ Granular cell tumor ○ Fibrovascular tumor* (3%) ○ Hemangioma (2%)



- Squamous papilloma (2%)
- Adenoma (1%)
- Inflammatory fibroid polyp (20%)
- Hamartoma
- Lipoma (2%)
- Cyst (10%)
- Neurofibroma (1%)

*also known as fibrovascular polyp, myxoma, angiofibroma, fibrolipoma, pedunculated lipoma, fibroepithelial polyp.

Abbreviation: GIST, gastrointestinal stromal tumor

Adapted from: Ginsberg G and Fleischer DE. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 969.

- The causes of multiple filling defects in the esophagus seen on barium swallow.

➤ Upper

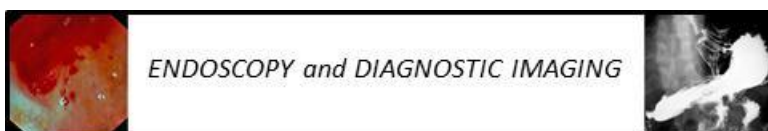
- Fibrovascular polyp
- Ectopic gastric mucosa

➤ Middle / lower

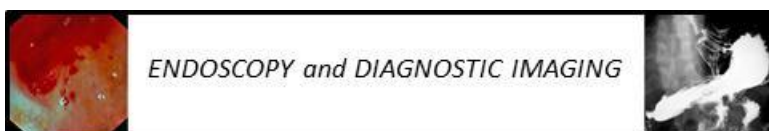
- GIST
- Duplication cyst
- Polypoid mass
 - Malignant
 - Squamous cell carcinoma
 - Adenocarcinoma
 - Lymphoma
 - Metastases
 - Carcinosarcoma
 - Benign
 - Adenoma
 - Papilloma
 - Gastroesophageal polyp (inflammatory)
- Swallow filling defects
 - Candidiasis
 - Glycogenic acanthosis
 - GERD

➤ Lower

- Thick folds-like filling defects
 - GERD
 - Varices



- Foreign body
 - Effervescent granules
- Infection
 - Candidiasis
- Tumor
 - Squamous cell cancer
 - Candidiasis
 - Papillomatosis
- Blood vessels
 - Varices
- The presenting symptoms for esophageal cancer.
- Esophagus
 - Dysphagia, odynophagia
 - Back or chest pain with/without swallowing
 - Halitosis
 - Tracheoesophageal fistula
 - Persistent substernal chest pain unrelated to swallowing
 - Hoarseness from recurrent laryngeal nerve involvement
 - Horner syndrome (miosis, ptosis, absence of sweating on ipsilateral face and neck)
 - Phrenic nerve involvement from hiccups
- Nerves
- Nodes
 - Supraclavicular adenopathy
- Systemic
 - Weight loss
 - Clubbing

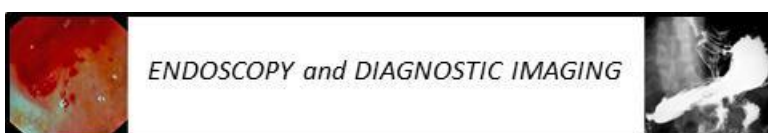


- The risk factors for esophageal squamous cancer and for adenocarcinoma.

	Adenocarcinoma	Squamous cell carcinoma
➤ Age	>50	>60
➤ Gender	M	M
➤ Alcohol	-	+
➤ Smoking	-	+
➤ GERD	+	-
➤ BE	+	-
➤ HIV	+	+
○ Previous head and neck squamous cell carcinoma		
○ Radiation therapy		
○ Lye ingestion		
○ Plummer-Vinson (Paterson-Kelly) syndrome		
○ Achalasia, Tylosis palmaris		
○ Nutritional deficiencies– riboflavin, niacin; high-starch diet without fruits and vegetables		
○ Nitrosamines; “bush teas” (diterpene phorbol esters)		
○ Gluten sensitive enteropathy (GSE)		

Abbreviations: BE, Barrett’s epithelium; GERD, gastroesophageal reflux disease

- The endoscopic imaging modalities for detecting esophageal neoplasia.
 - High resolution/high-definition/magnification endoscopy – white light high resolution endoscopy (HRHDME)
 - Chromoendoscopy (CE) (combined with HRHDME) – Lugol’s sphincter, toluidine blue, methylene blue, indigo carmine, acetic acid, crystal violet
 - Narrow band imaging (NBI)
 - FICE (Fujinon intelligent chromendoscopy; computed interval chromendoscopy)
 - Point spectroscopy – fluorescence, elastic scattering, RAMAN, multimedial
 - Autofluorescence imaging (LIFE, light -induced fluorescence endoscopy [FE]), drug-induced FE, video autofluorescence imaging)
 - Optical coherence tomography (OCT)
 - Confocal endomicroscopy
 - EUS

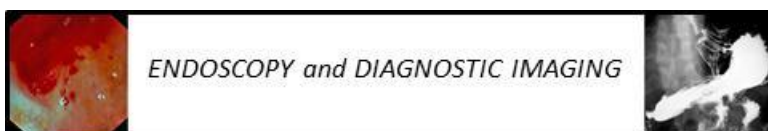


Abbreviations: CE, chromoendoscopy; EUS, endoscopic ultrasound; FE, fluorescence endoscopy; FICE, intelligent chromoendoscopy; CIC, computed interval chromosendoscopy; HRHDME, white light high resolution endoscopy; LIFE, light -induced fluorescence endoscopy; OCT, optical coherence tomography

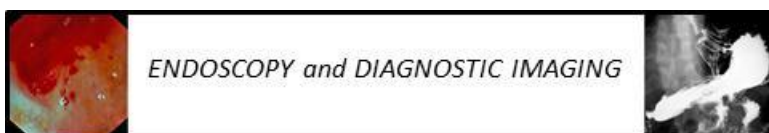
Printed with permission: Curvers WL, Kiesslich R, Bergman JJ. *Best Prac Res Clin Gastroenterol* 2008; 22(4):687-720.

Diagnostic imaging

- Perforation
 - Squamous carcinoma
 - Mass
 - Not bulky
 - Irregular contour
 - Abrupt shelf (shouldered) edge
 - Ulcer (does not project beyond) the expected location of the normal esophageal mucosa
 - GE junction not usually crossed
 - Mid esophagus
- Adenocarcinoma
 - Distal thick wall (> 3 mm; nonspecific sign)
 - Hiatus hernia (Barrett, reflux)
 - Bulky polypoid tumor
 - Gastric invasion
 - Enlarged nodes (> 1.5 cm) suggests metastases
- Metastases
 - Nodular or polypoid extrinsic
 - Mass displaces lumen
 - Mucosal or extramucosal
 - Middle (mediastinal node compression)
 - Enlarged nodes
 - 1^o – stomach, lung, breast
 - CT – metastases: no attenuation
- Lymphoma
 - every size / shape
 - ulcerated mass
 - bulky, polypoid
 - submucosal infiltration / mass
 - thick varicoid folds
 - nothing specific



- Adenoma
 - usually within BE (distal)
- Papilloma
 - looks like adenoma
 - fibrovascular excrescences covered with squamous epithelium
- Carcinosarcoma (spindle cell carcinoma)
 - mid / lower
 - bulky, polypoid, intraluminal
 - may have a stalk
 - may expand the lumen (because of large size)
- Intramural (submucosal) tumors
 - Stromal
 - Hemangioma
 - Fibroma
 - Neuroma
 - Duplication cyst
 - Lymphoma
 - Neurofibroma
 - Lipoma
- Fibrovascular tumors
 - long (> 7 cm)
 - contains fat
 - on CT
 - does not enhance with IV contrast material
- The differential diagnosis of dysphagia and odynophagia in persons with HIV/AIDS.
- Infection
 - Candida albicans (CMV)
 - Herpes simplex (HSV)
 - Histoplasma capsulatum
 - Mycobacterium avium complex (MAC)
 - Cryptosporidium spp.
 - PCP
- Malignancy
 - Adenocarcinoma
 - Lymphoma
 - Kaposi's sarcoma
 - Squamous cell carcinoma



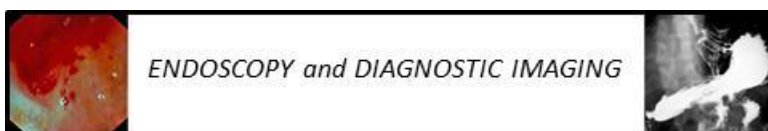
- Treatment
 - Pill-induced esophagitis
 - HAART-associated mucositis
 - GERD (idiopathic may be more common)
 - Idiopathic

- Idiopathic ulceration

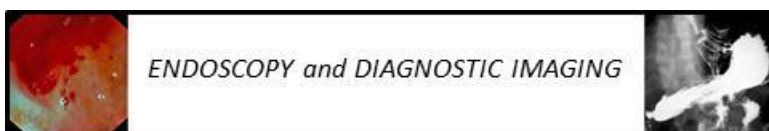
Abbreviations: CMV, cytomegalovirus; HSV, herpes simplex virus; MAC, mycobacterium avium complex

Diagnostic imaging

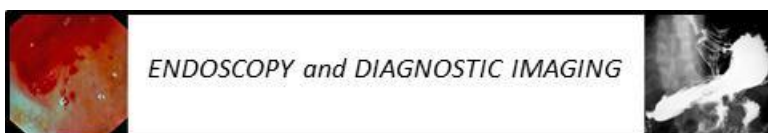
- Miscellaneous
- Differential:
 - Bulky polypoid tumor
 - Adenocarcinoma
 - Spindle cell (carcinosarcoma)
 - Lymphoma
- Thick, distorted folds
 - Extension into submucosa
 - Uphill (lower esophagus) varices serpentine
 - Downhill (upper esophagus) tubular
- Inflammatory gastroesophageal polyp
 - enlarged gastric fold extending from upper stomach to lower esophagus
 - clubbed, bulbous
- Gastrointestinal
 - stromal tumor (GIST)
 - does not arise from a stalk
 - bulky, intraluminal mass
 - smooth surface
 - obtuse angle between mass and lumen (two signs suggesting submucosal: [intramural] smooth, obtuse)
 - common
 - mid/lower
 - single (96%)
- Duplication cyst
 - Attenuation with water



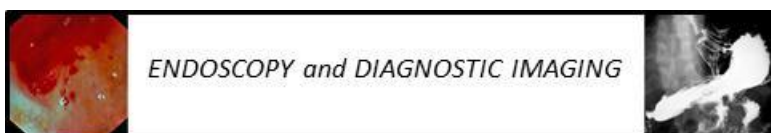
- Does not enhance with IV contrast material
 - Lined with squamous epithelium, have a smooth muscle wall
 - Oblique with esophageal contour
 - Mass may displace lumen
 - Surface - well – demarcated mass
 - Looks like GIST on contrast esophagography (barium)
- Varices
- “Uphill”
 - Distal
 - Linear
 - Serpiginous filling defects
 - Scalloped contour
 - Change size/ shape
 - May be present also in gastric fundus
 - Portal vein → L.gastric vein → azygous / hemiazygous system → SVC
 - “Downhill”
 - Upper
 - Filling defects
 - Superior vena cava (SVC) obstruction →
 - Azygous / hemiazygous system →
 - Systemic circulation (no PHT)
- Ectopic gastric mucosa
- Upper esophagus
 - 2 shallow indentations
 - Small, < 2 cm diameter
- Foreign bodies
- Intraluminal filling defect
 - Upper chicken bone (best seen on lateral film of cervical region)
 - Lower meat
- Diverticula
- Upper
- Lateral pharyngeal pouch
 - Zenker
 - Killian-Jamieson
- Middle
- Pulsion
 - Traction
 - Intramural pseudodiverticulosis

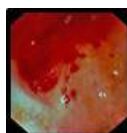


- Lower
 - Epiphrenic
- Hernia
- Supine
- Paraesophageal
- Intramural pseudodiverticulosis
 - Tiny out pouching
 - Segmental or diffuse
 - Associated stricture in 90%
 - Upper/mid esophagus
 - Neck of out pouching may not appear to communicate with the lumen, as they actually do (arise from dilated submucosal glands)
- Lateral pharyngeal pouches
 - Smooth out pouching
 - Both sides of esophagus
 - Arise in an area of thyrohyoid membrane devoid of overlying muscle
- Zenker diverticulum
 - Unilateral round out pouching of barium in the posterior wall of the cervical esophagus from herniation of mucosa between the oblique and horizontal fibers of the esophageal wall (Killian triangle)
 - Prominence of cricopharyngeal bar below muscle
- Pseudo – Zenker diverticulum
 - Small out pouching of barium during a pharyngeal contraction wave and prominent cricopharyngeal muscle
 - Above the muscle
- Pulsion diverticulum
 - Round
 - Caused by motor disorder of esophagus
 - Does not empty with peristalsis (false diverticulum, pulsion of mucosa, no muscle in wall for peristalsis)
- Killian – Jamieson diverticulum
 - Bilateral round out pouching of barium anteriorly off the lateral wall of the cervical esophagus
 - Below the cricopharyngeal muscle on the cricoids cartilage, and lateral to the suspensory ligament which insert on the cricoids cartilage (Killian-Jamieson space)



- Traction diverticulum
 - Unilateral out pouching of barium in mid esophagus
 - Triangular – shaped
 - Fibrosis in periesophageal tissues from TB
 - Empty with a peristaltic contraction
- Epiphrenic diverticulum
 - A type of pulsion diverticulum in lower esophagus
 - Associated with motor disorder such as achalasia





ENDOSCOPY and DIAGNOSTIC IMAGING

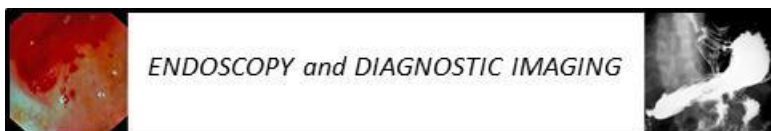


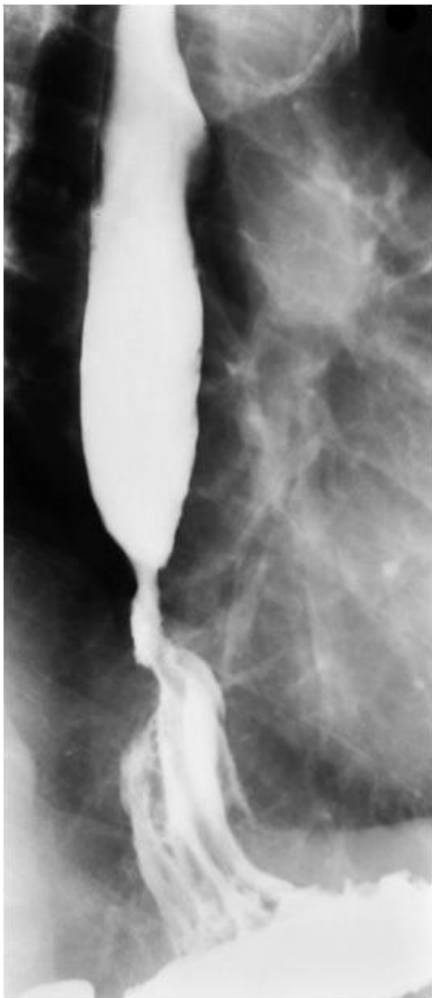
ESOPHAGUS DIAGNOSTIC IMAGING

CLINICAL SKILLS

Self-assessment

**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**



Case 1

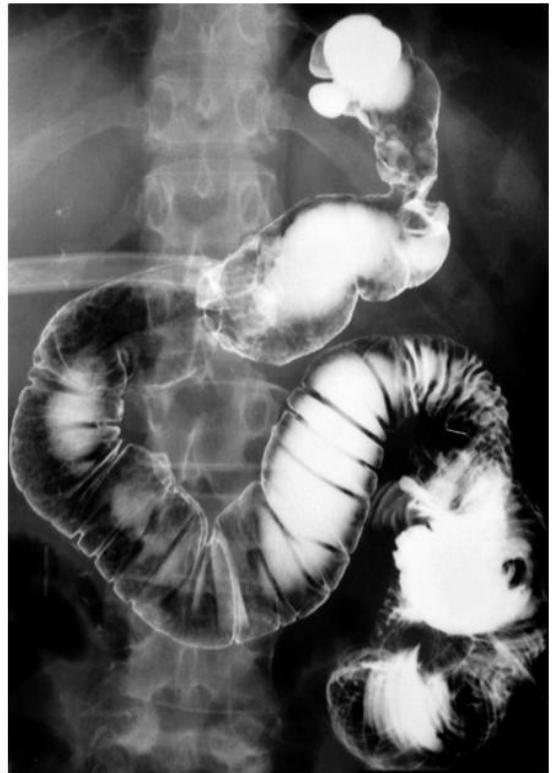
65 year old female presents with dysphagia.

Case 2

52 year old male presents with chest pain.

Case 3

68 year old male presents with halitosis.

Case 4

25 year old male drank lye, and 7 days later developed dysphagia.

Case 5

61 year old male presents with one year history of progressive dysphagia for solids.

Case 6

Patient presents with Raynaud's phenomenon and dysphagia for liquids and solids

Case 7

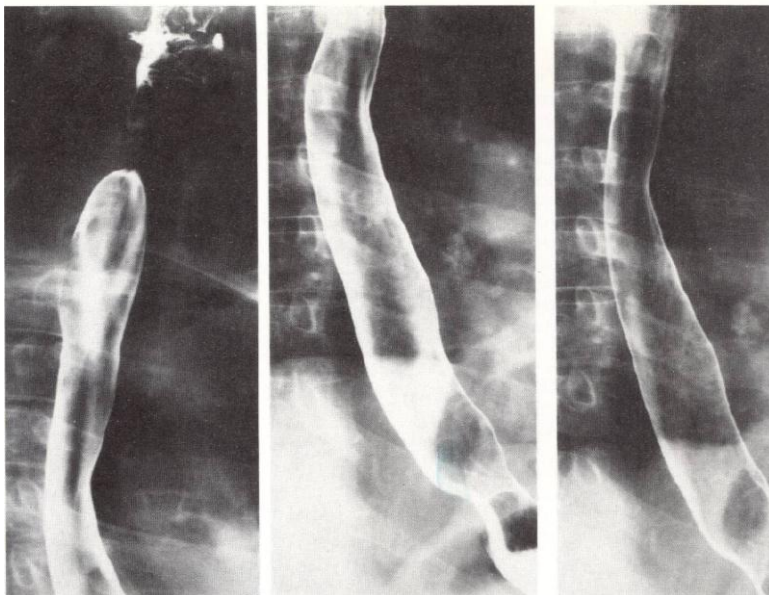
25 year old male presents with globus sensation.

Case 8

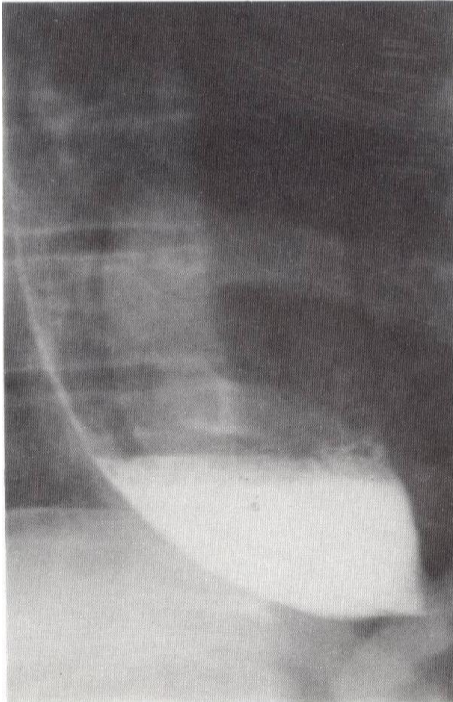
60 year old male with chronic dyspepsia presents with progressive dysphagia for solids.

Case 9

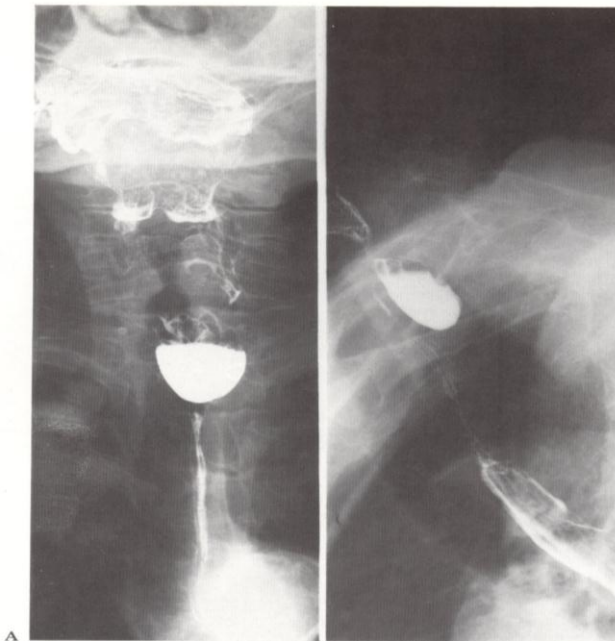
72 year old female presents with dysphagia and weight loss.

Case 10

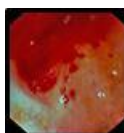
35 year old woman with Raynaud's phenomenon and dysphagia

Case 11

Dysphagia for liquids, halitosis and regurgitation in a 60 year old man

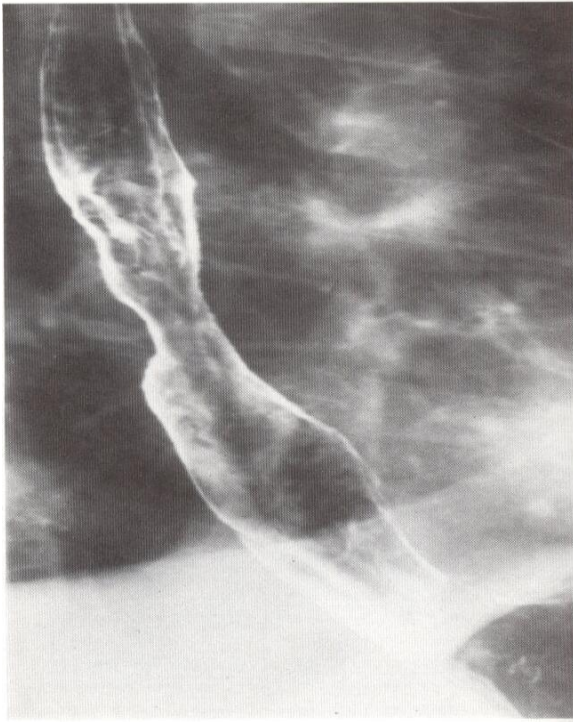
Case 12

75 year old man
complaining of
dysphagia and
regurgitation

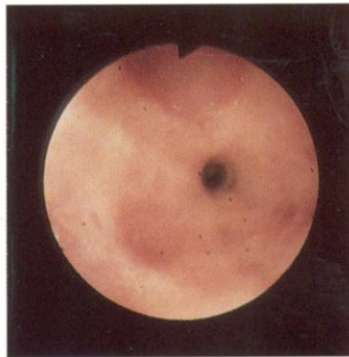


ENDOSCOPY and DIAGNOSTIC IMAGING

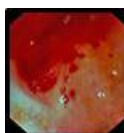


Case 13

70 year old Caucasian male with 15 year history of regurgitation and heartburn occurring at least three times a week, presents with solid food dysphagia



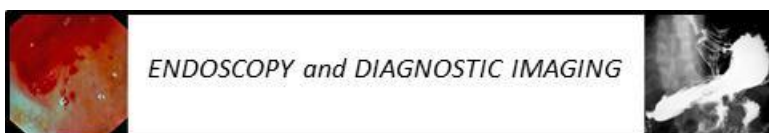
B

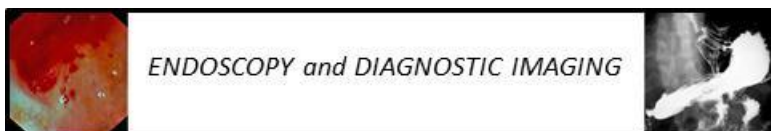


Diagnostic imaging answers**Esophagus (barium swallow and/ or upper GI series)**

1. Hiatal hernia, distal stricture, irregular margins: tumor plus esophagitis.
2. Corkscrew esophagus.
3. Zenker's diverticulum.
4. Gastric stricture, fistula from esophagus to L. stem bronchus.
5. Polypoid esophageal carcinoma.
6. Dilated mid body of esophagus, smooth distal narrowing (scleroderma).
7. Multiple esophageal filling defects (esophageal varices).
8. Hiatus hernia, dilated esophagus, distal narrowing with irregular margins (tumor).
9. Diffuse infiltration of distal stomach, compatible with linitis plastica.
10. Systemic sclerosis.
11. Achalasia, food retention.
12. Pharyngeal pouch.
13. Esophageal stricture.

Please compare your findings with those described in the previous material.





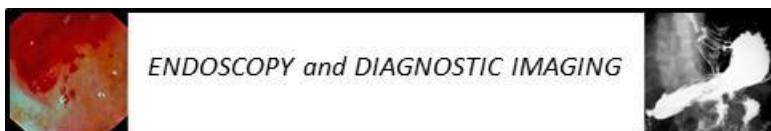
ESOPHAGUS ENDOSCOPIC IMAGING

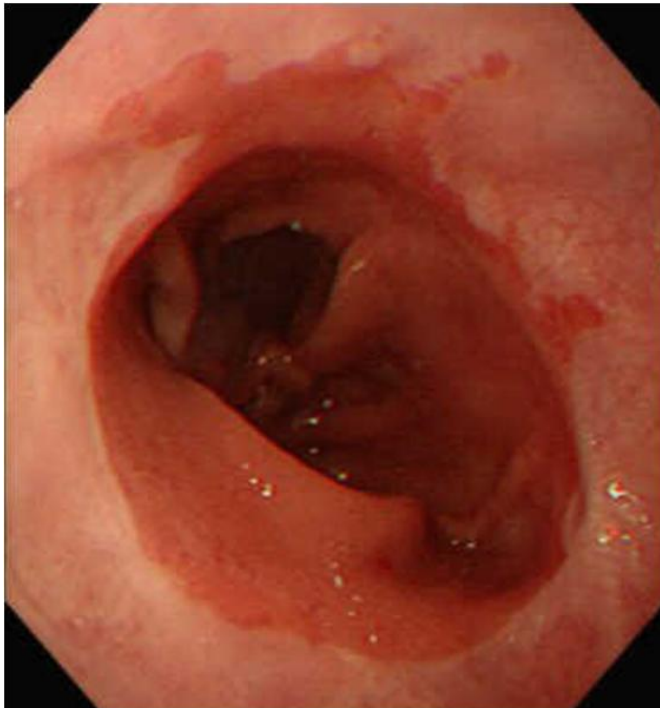
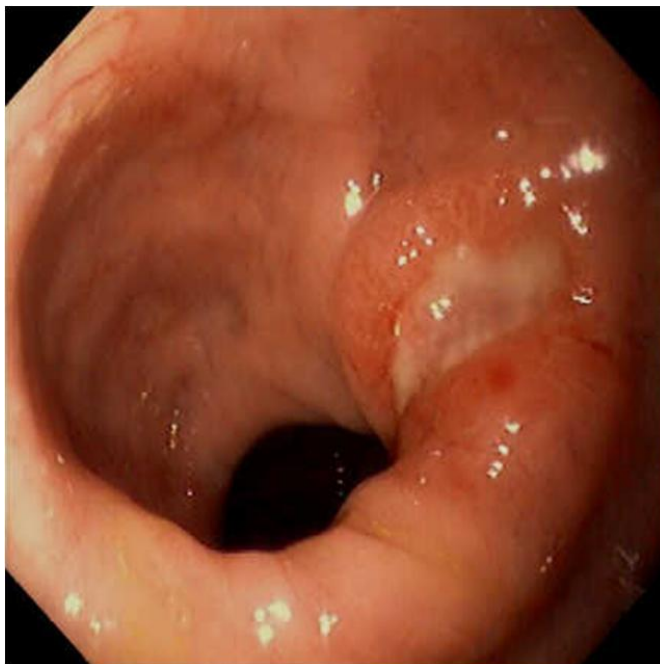
CLINICAL SKILLS

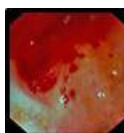
Self-assessment

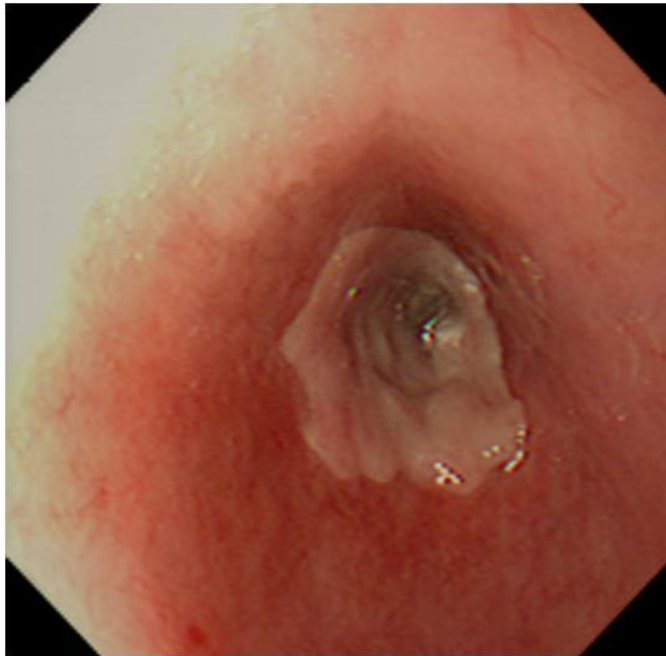
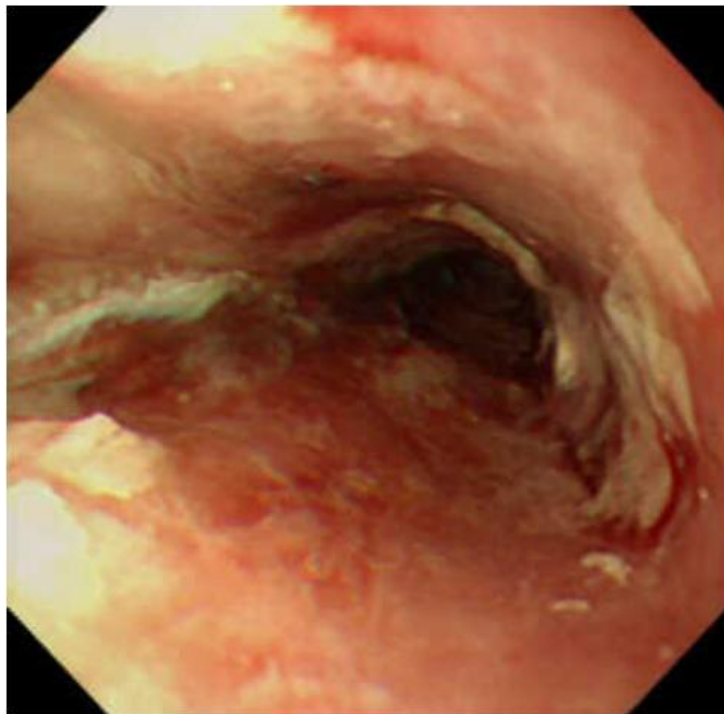
**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**

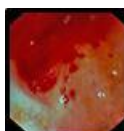
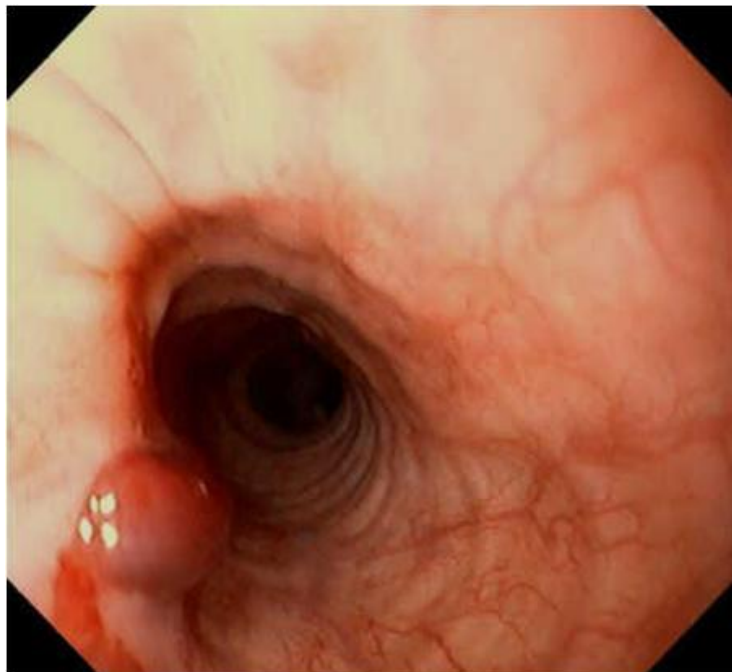
*Provided through the courtesy of Dr. Edgar Jaramillo, Center of
Gastrointestinal Disease, Ersta Hospital, Stockholm, Sweden*

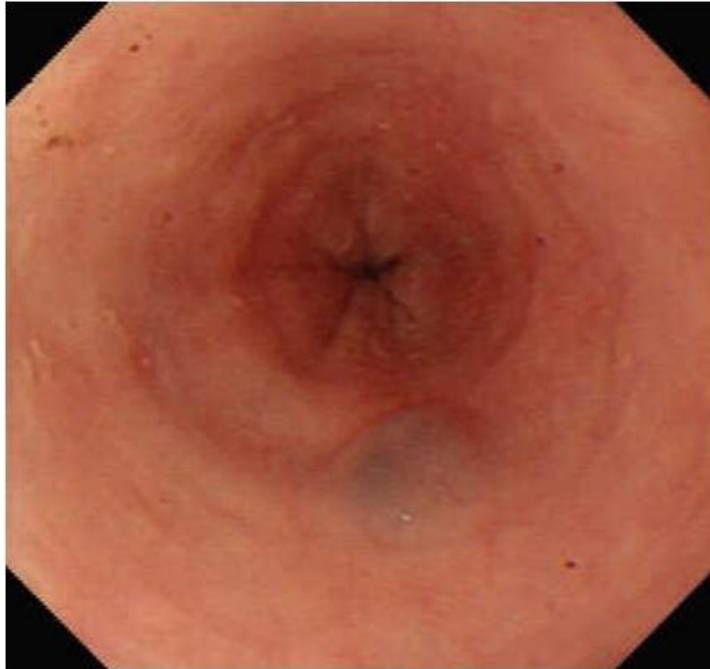
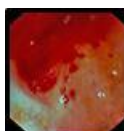
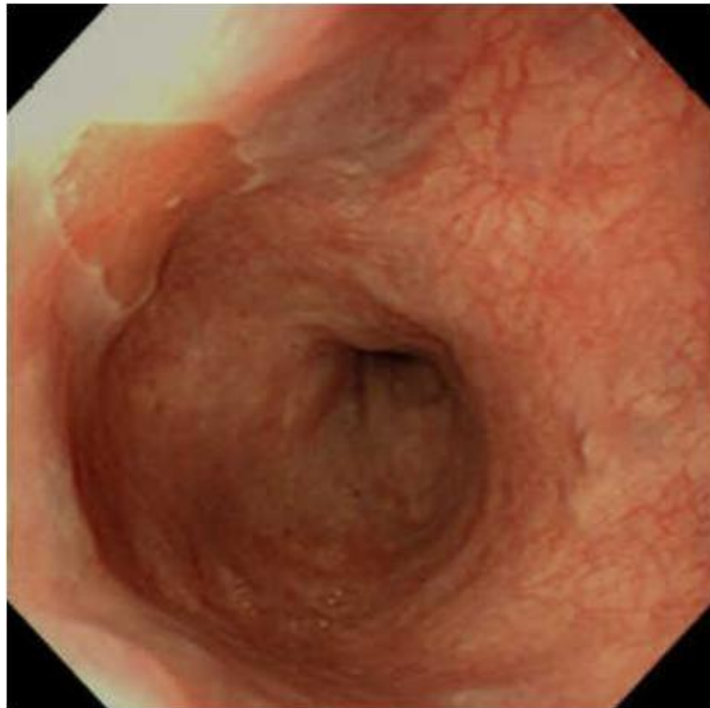


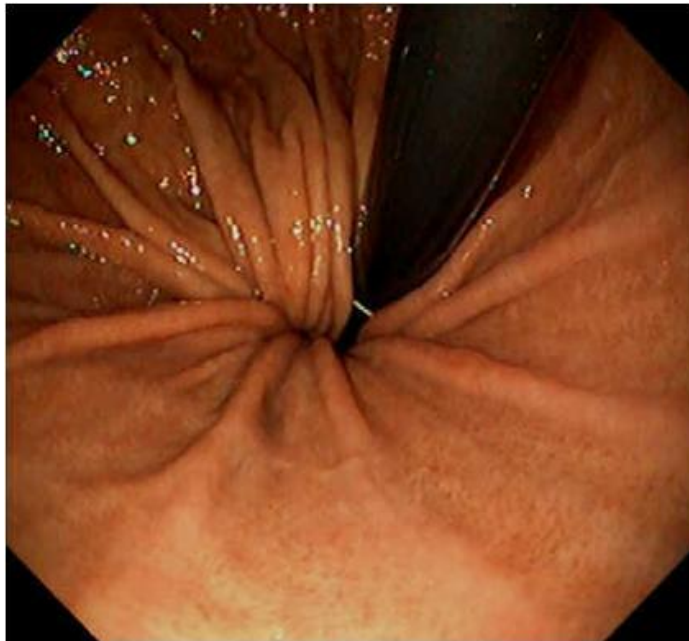
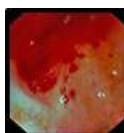
Case 1**Case 2**

Case 3**Case 4**

Case 5**Case 6**

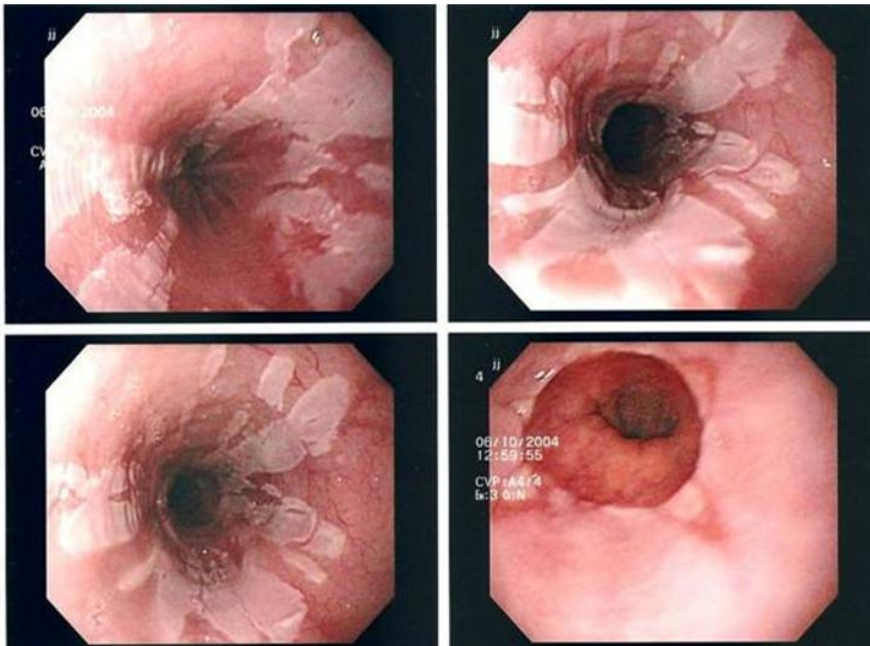
Case 7**Case 8**

Case 9**Case 10**

Case 11**Case 12**

Case 13**Case 14**

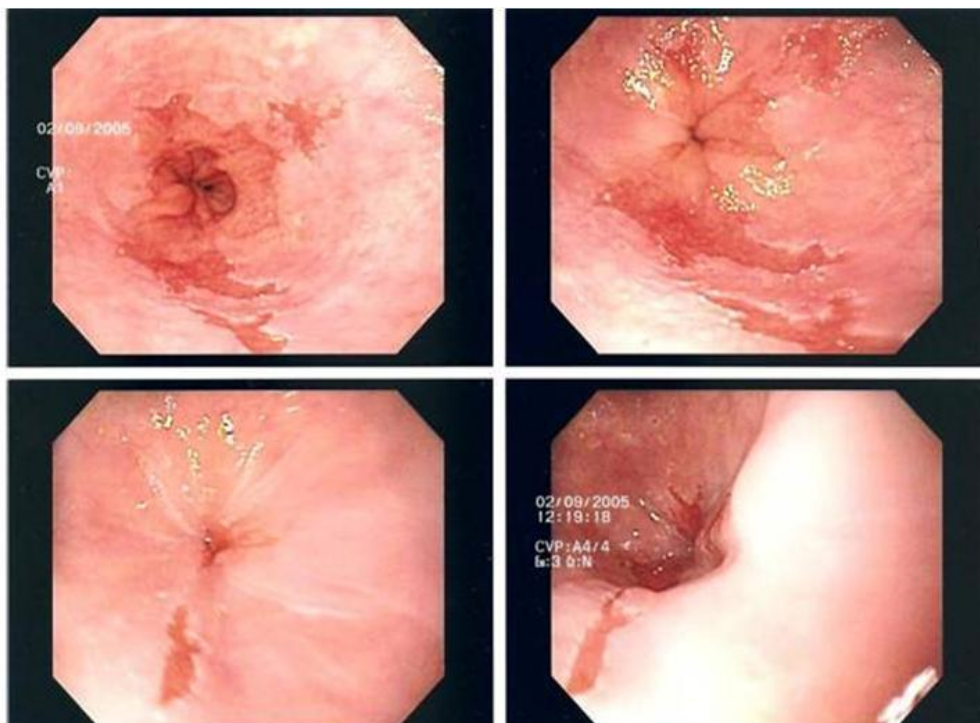
A 48 year old Caucasian man with a long history of severe gastroesophageal reflux symptoms. Please describe the esophageal endoscopic findings, and outline your management.



The endoscopy photographs were provided through the courtesy of Dr. C. Noel Williams, Dalhousie University and University of Alberta.

Case 15

A 52 year old man on tacrolimus for a cardiac transplant for hereditary cardiomyopathy presents with new symptoms of GERD. Please describe the endoscopic findings, give a differential for the esophageal endoscopic findings, and outline your management.

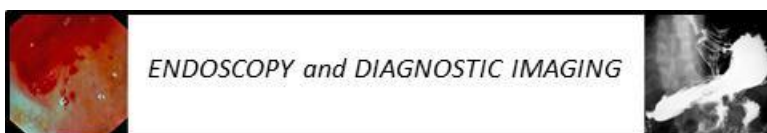


The endoscopy photographs were provided through the courtesy of Dr. C. Noel Williams, Dalhousie University and University of Alberta.

SO YOU WANT TO BE A GASTROENTEROLOGIST?

Q. What are the cause of an absent gastric air bubble?

- A.
- Large hiatus hernia
 - Achalasia
 - Stomach full of food/fluid
 - Large, upper abdominal mass
 - splenomegaly



Esophageal endoscopy answers

1. Barrett's esophagus
2. Barrett's ulcer
3. Zenker's diverticulum
4. Candida esophagitis
5. Radiation esophagitis
6. Viral esophagitis
7. Fundoplication
8. Hematoma
9. Hemangioma
10. Heterotopic gastric mucosa
11. Paraesophageal hernia
12. Peptic stricture
13. Submucosal tumor
14. Suspected Barrett's, biopsies negative
15. PTLD (Post-transplantation lymph proliferative disorder)

SO YOU WANT TO BE A GASTROENTEROLOGIST?

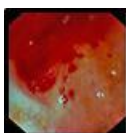
Q1. Metastases to the lung are usually seen as a few large deposits. From what primary tumors are the metastases to the lung usually multiple and small?

A1. Lung metastasis from primary cancers of

- Bronchus
- Stomach

Q2. What is the difference between mottling and military mottling on a chest X-ray?

- A2.
- Mottling is multiple, discrete semiconfluent shadows, < 5 mm.
 - Military mottling is multiple, discrete, bilateral shadows, < 2 mm.

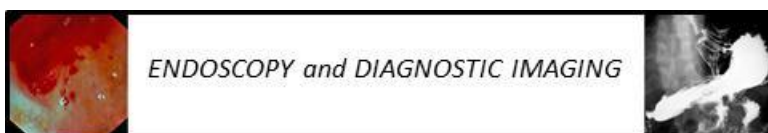


This material was kindly provided by Dr. D. Sadowski,(University of Alberta)

STANDARD MANOMETRY

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Pre and Post Fundo mechanical obstruction “pre-bolus obstruction pattern”	88
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Scleroderma Pattern	104
Achalasia	107
Inco-ordinate PE	111



Normal study

Clinical History:

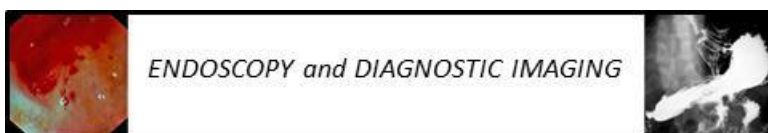
Presenting Symptom: heartburn

Other Symptom:

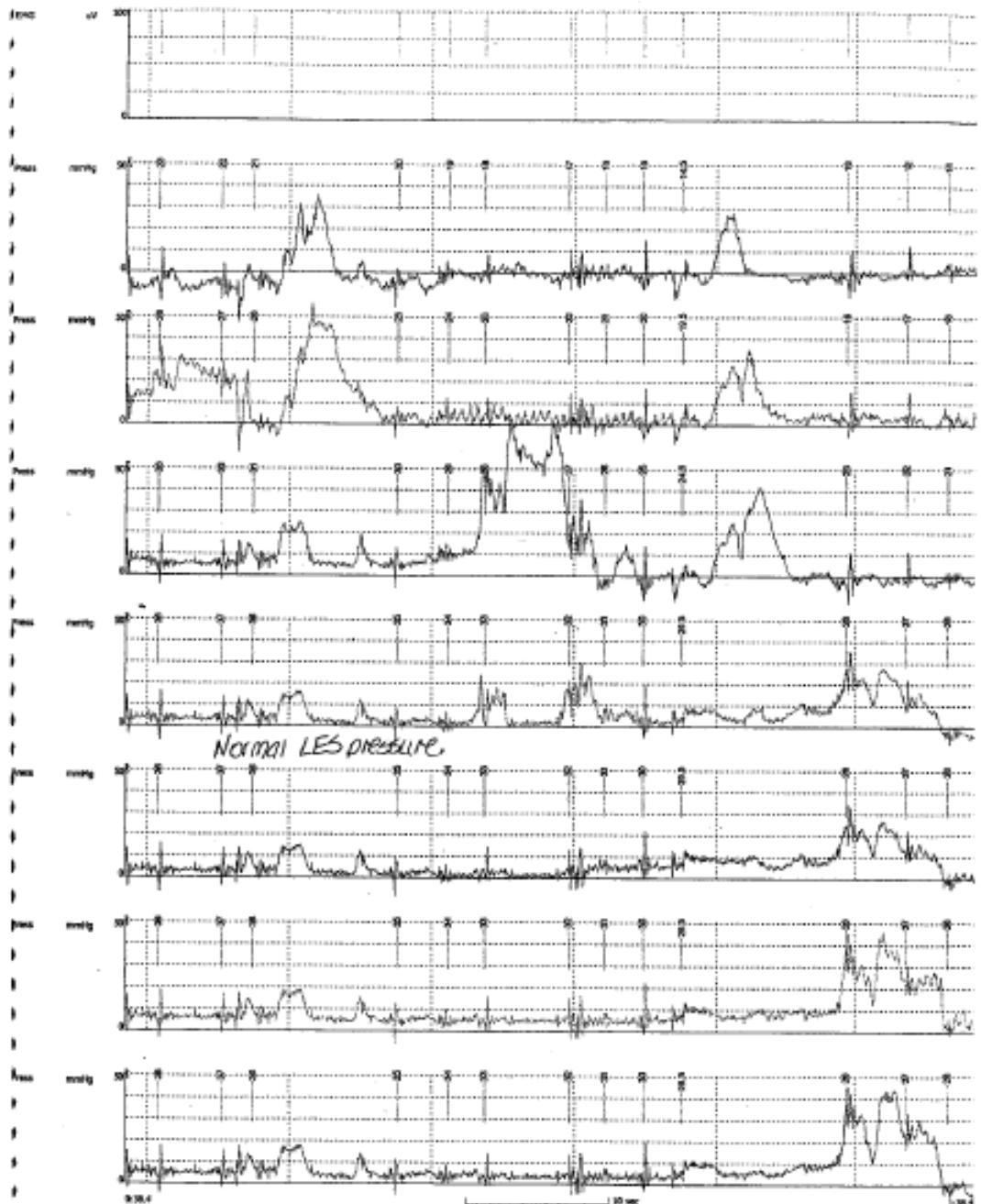
Lower esophageal sphincter (Normal values in brackets)	Esophageal body: (Normal values in brackets)
Resting pressure: 21 mm Hg (16-30)	Peristaltic contractions: 100% (>80%)
Relaxation duration: 5.3 seconds (>2)	Simultaneous contractions: 0% (<20%)
% Relaxation: 93% (80-100%)	Mean contraction amplitude: 73 mm Hg (30-180)
Residual Pressure: 1.5 mm Hg (<8)	Mean contraction duration: 2.5 seconds (<5.8)
	Low amplitude contractions: 0% (<30%)
	Spontaneous activity between swallows: none

- **Acid Infusion Test:** Not done
- **Pharyngo-Esophageal Sphincter (PE):** Not done
 - Resting Pressure: mm Hg (40-150)
 - Pharyngeal contraction pressure: mm Hg (40-150)
 - Coordination:

Summary and Conclusions: Difficult study to perform. Patient upright. Normal LES pressure. Normal body study. Peristalsis present. Essentially normal study.

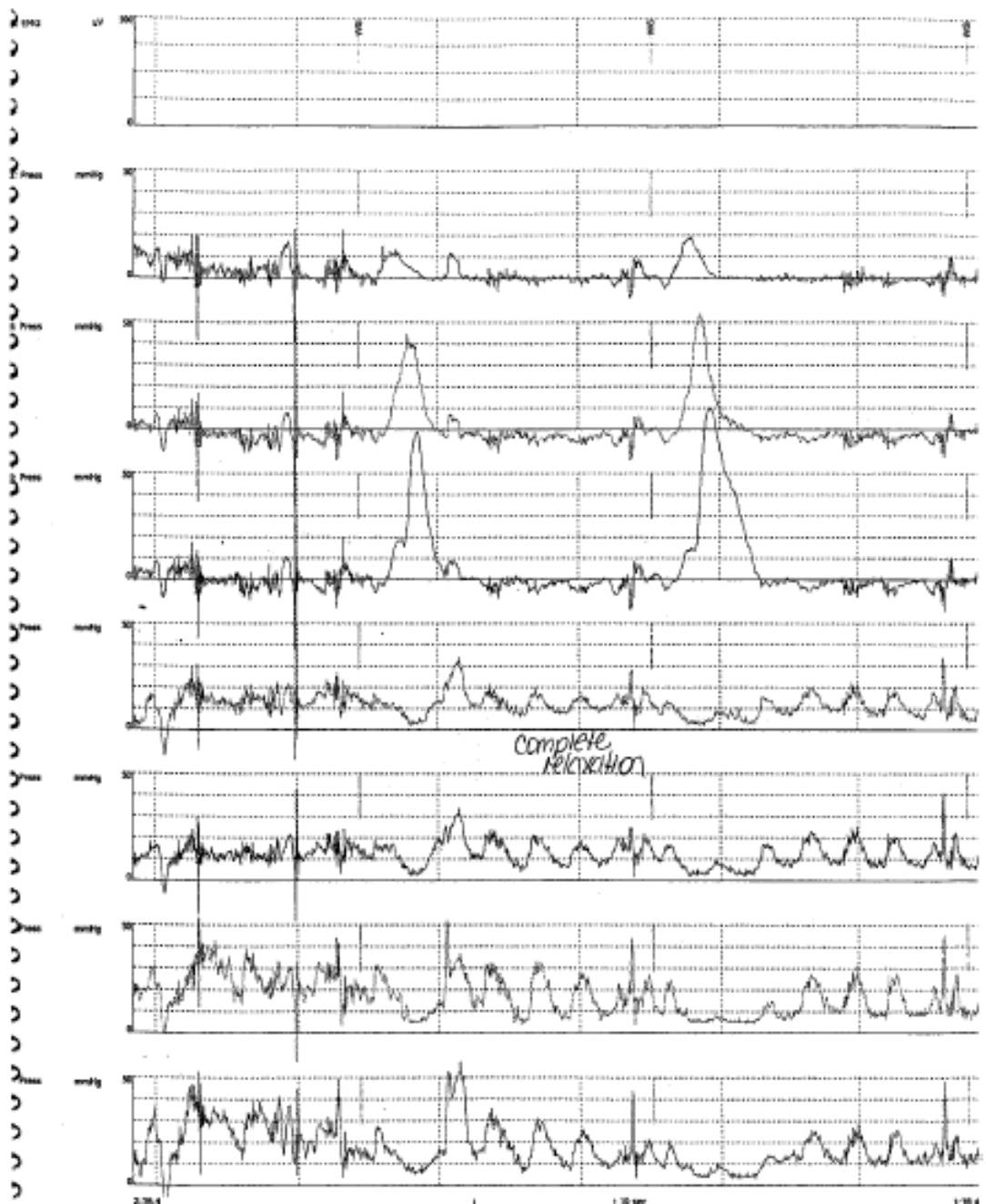


Channel Water Perfused Esophageal Manometry

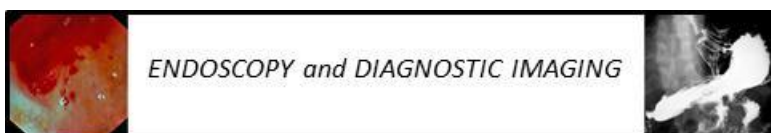


Normal Study

Channel Water Perfused Esophageal Manometry



Normal Study



Channel Water Perfused Esophageal Manometry



Normal Study

Hiatus hernia

Clinical History:

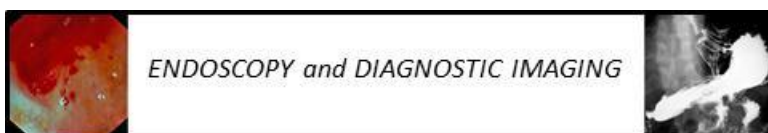
Presenting Symptom: regurgitation

Other Symptoms: heartburn, hiatus hernia

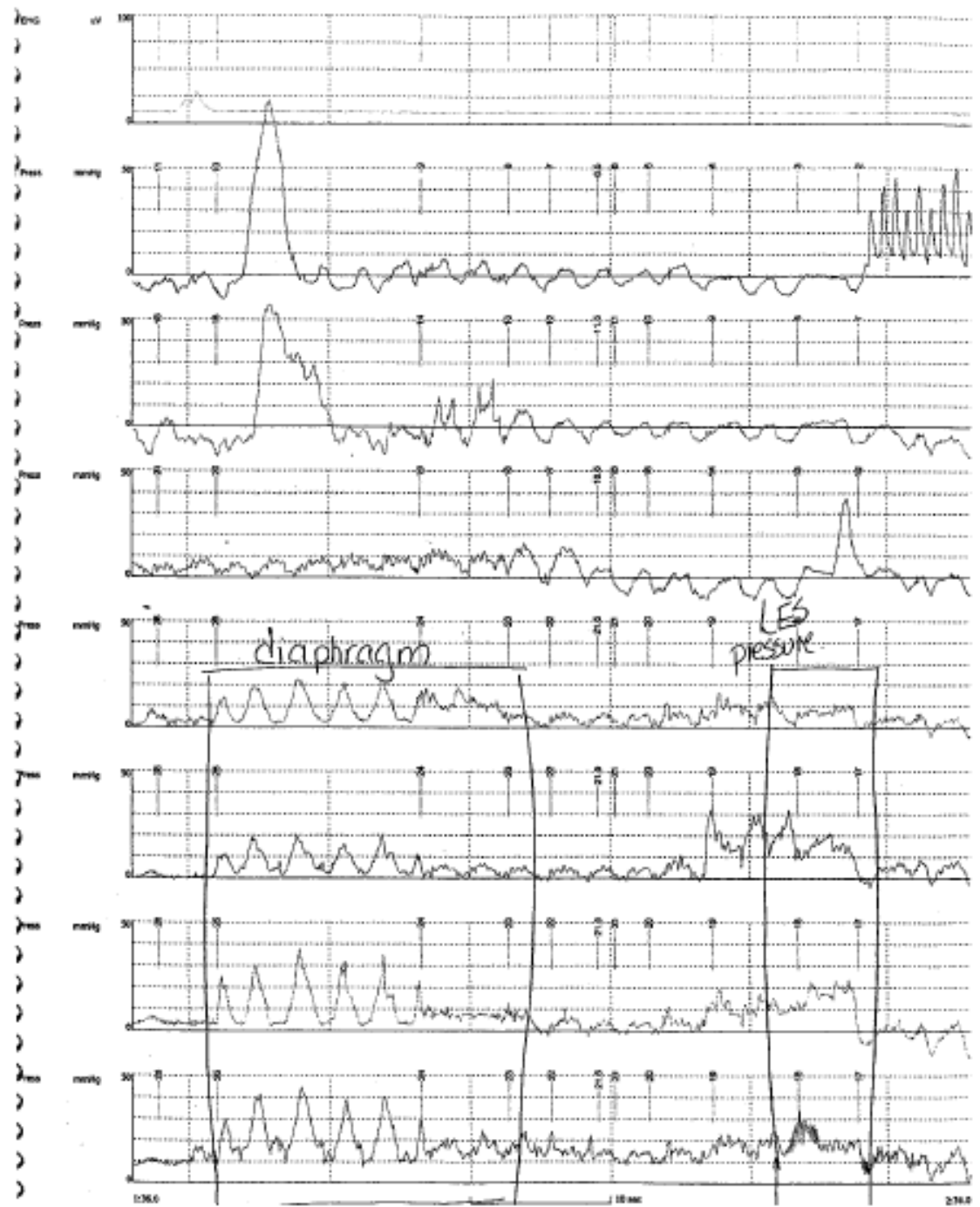
Lower esophageal sphincter (Normal values in brackets)	Esophageal body: (Normal values in brackets)
Resting pressure: 12 mm Hg (16-30)	Peristaltic contractions: 100% (>80%)
Relaxation duration: 8.5 seconds (>2)	Simultaneous contractions: 0% (<20%)
% Relaxation: 100% (80-100%)	Mean contraction amplitude: 156 mm Hg (30-180)
Residual Pressure: 0 mm Hg (<8)	Mean contraction duration: 3.4 seconds (<5.8)
	Low amplitude contractions: 0% (<30%)
	Spontaneous activity between swallows: none

- **Acid Infusion Test:** Not done due to what appears to be a hiatus hernia
- **Pharyngo-Esophageal Sphincter (PE):**
 - Resting Pressure: 21.1 mm Hg (40-150)
 - Pharyngeal contraction pressure: 52.8 mm Hg (40-150)
 - Coordination: Yes

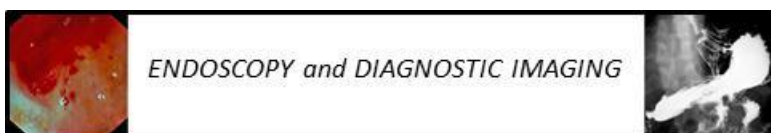
Summary and conclusions: Patient has what appears to be a hiatus hernia. Feeble LES pressure. Minor motor abnormality body of esophagus. Peristalsis present with 30% of solicited swallows of increased amplitude in distal esophagus. Feeble PE.



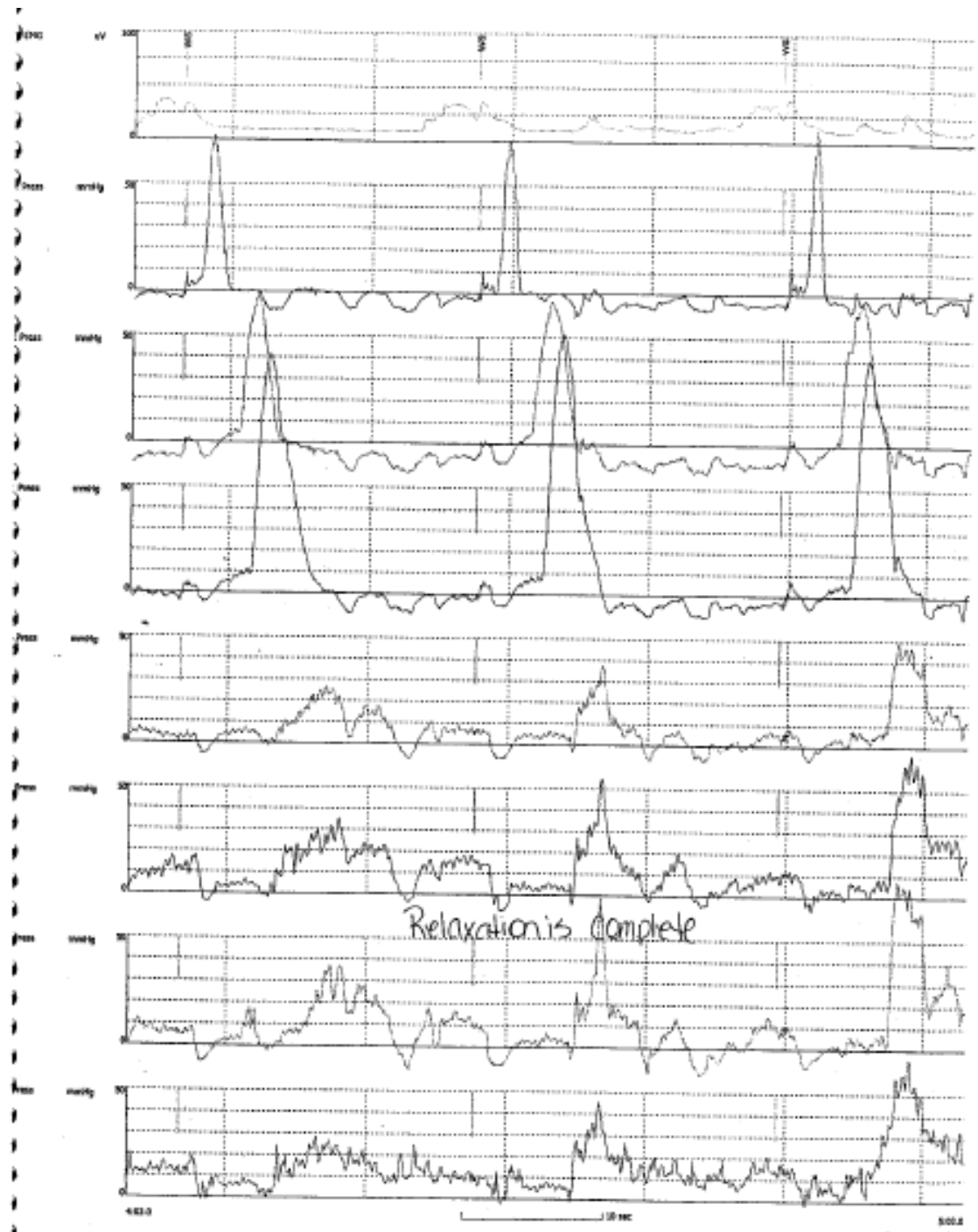
Channel Water Perfused Esophageal Manometry



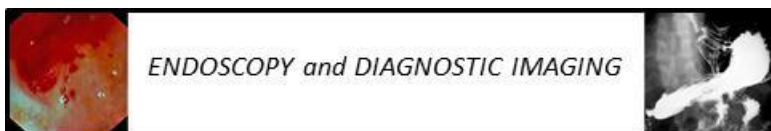
Hiatus hernia



Channel Water Perfused Esophageal Manometry



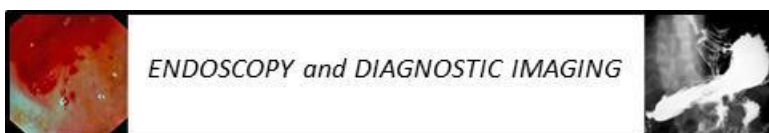
Hiatus hernia



Channel Water Perfused Esophageal Manometry



Hiatus hernia



Pre and post fundus mechanical obstruction

“PRE-BOLUS OBSTRUCTION PATTERN”

Clinical History:

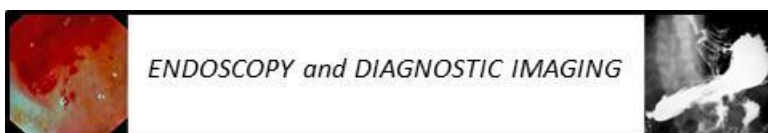
Presenting Symptom: dysphagia in epigastric area

Other Symptoms: fundus in May 2005, dilation x 2

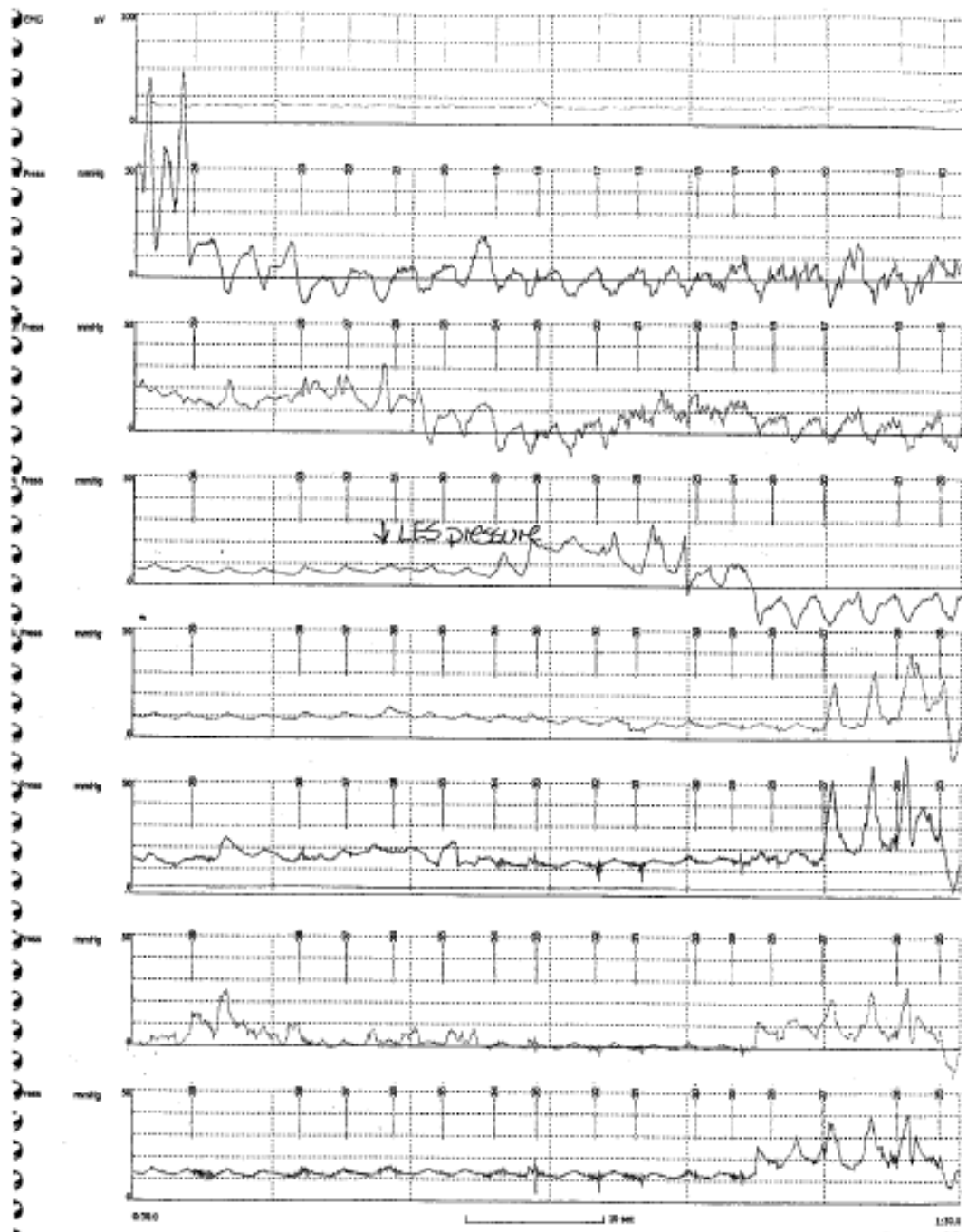
Lower esophageal sphincter (Normal values in brackets)	Esophageal body: (Normal values in brackets)
Resting pressure: 22 mm Hg (16-30)	Peristaltic contractions: 100% (>80%)
Relaxation duration: 11.3 seconds (>2)	Simultaneous contractions: 0% (<20%)
% Relaxation: 66% (80-100%)	Mean contraction amplitude: 120 mm Hg (30-180)
Residual Pressure: 11.3 mm Hg (<8)	Mean contraction duration: 5 seconds (<5.8)
	Low amplitude contractions: 0% (<30%)
	Spontaneous activity between swallows: none

- **Acid Infusion Test:** not done
- **Pharyngo-Esophageal Sphincter (PE):** not done
 - Resting Pressure: mm Hg (40-150)
 - Pharyngeal contraction pressure: mm Hg (40-150)
 - Coordination:

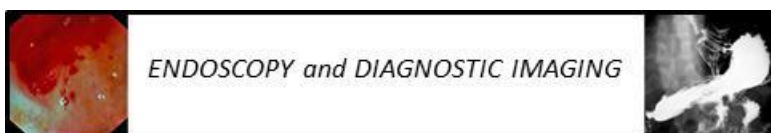
Summary and Conclusion: Normal LES pressure. Relaxation is incomplete. Significant motor abnormality body of esophagus. Peristalsis present with 70% of solicited swallows simultaneous from mid to distal esophagus, 40% of swallows are of increased duration in distal esophagus. Compatible with pre-bolus obstruction pattern. Rule out mechanical obstruction.



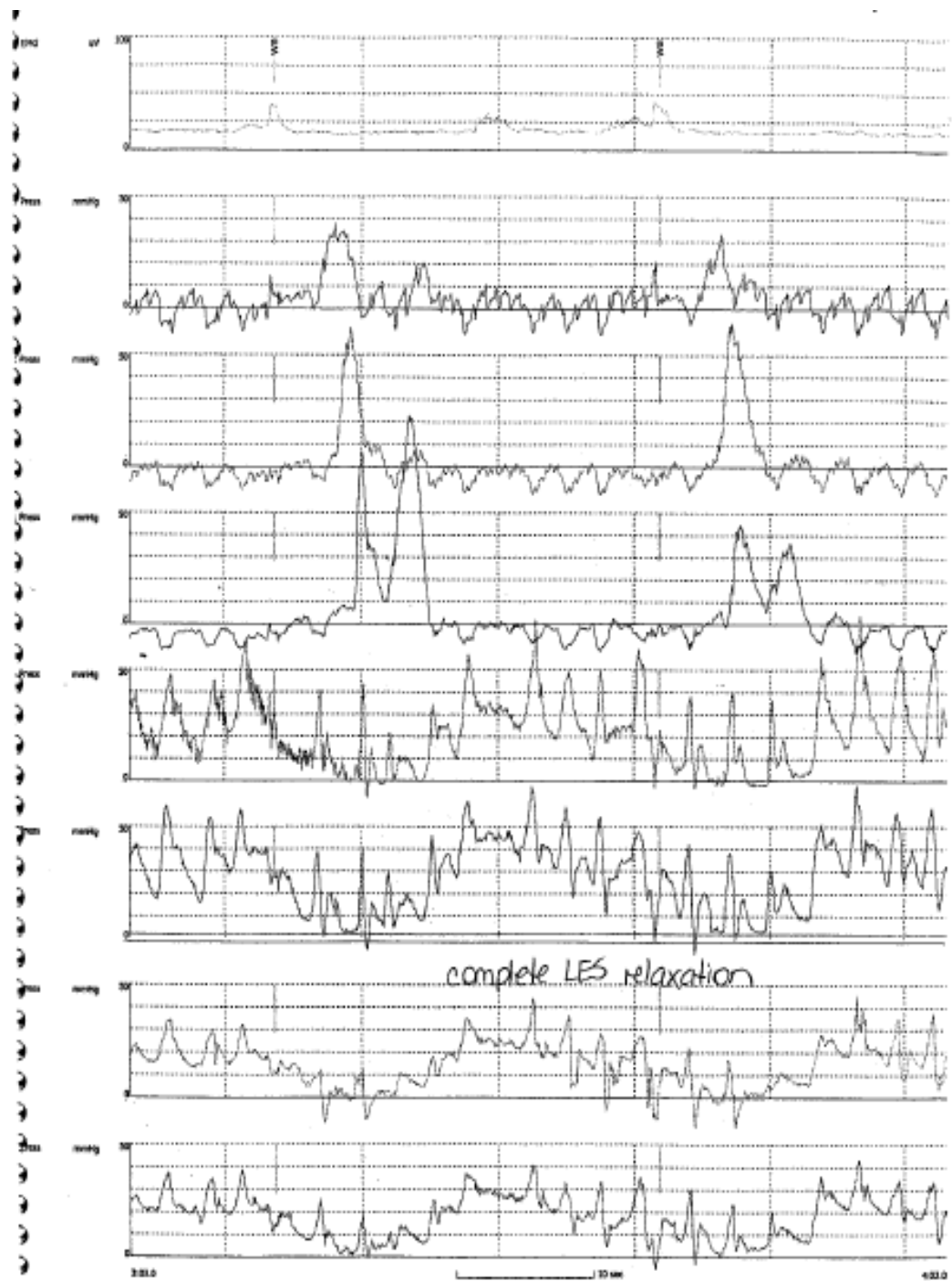
Channel Water Perfused Esophageal Manometry



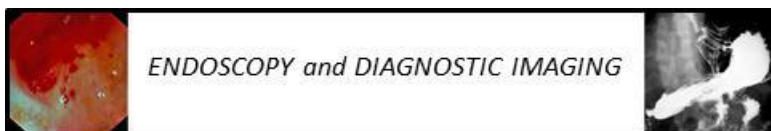
Pre and post fundo mechanical obstruction" pre-bolus obstruction pattern



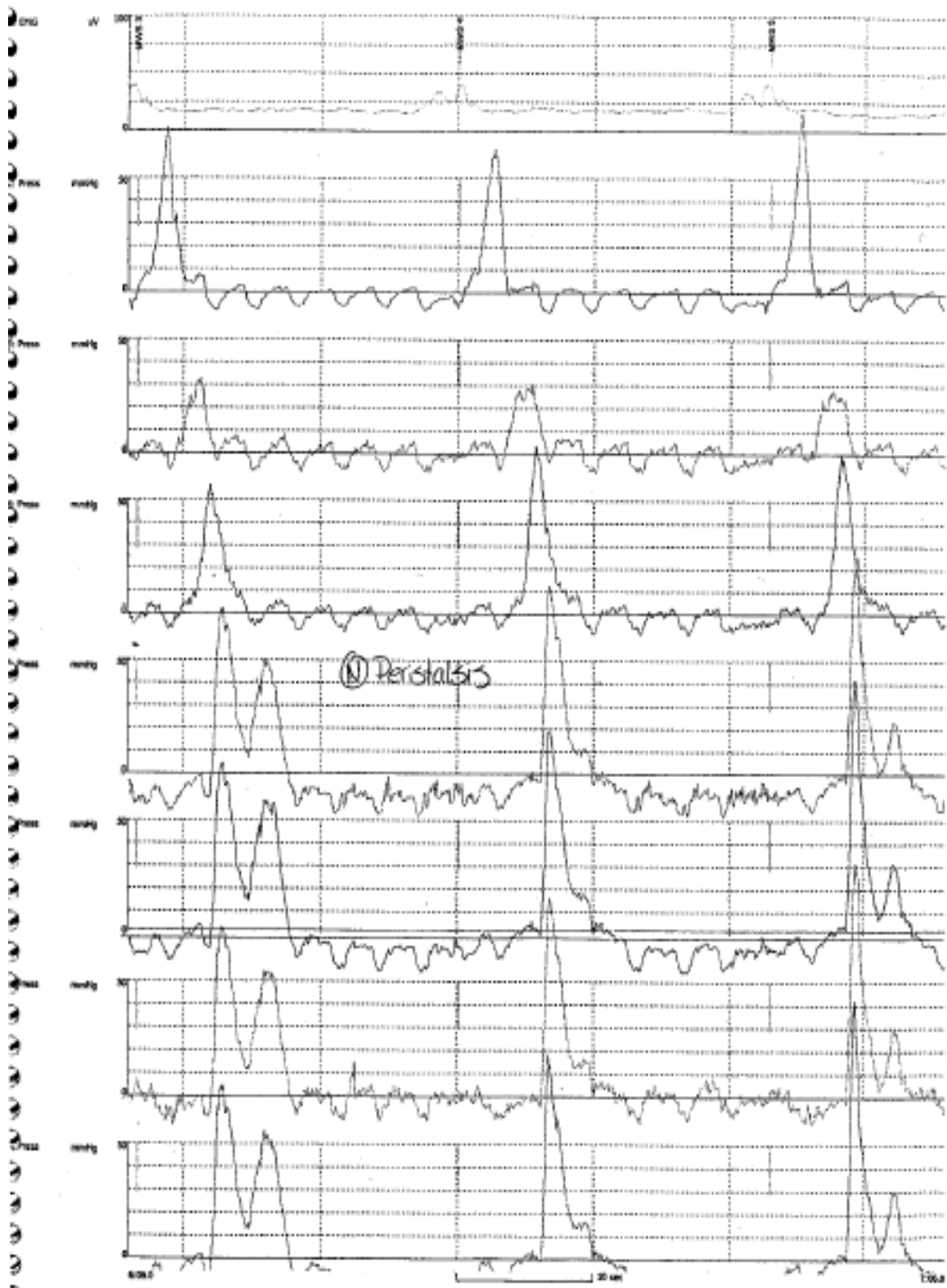
Channel Water Perfused Esophageal Manometry



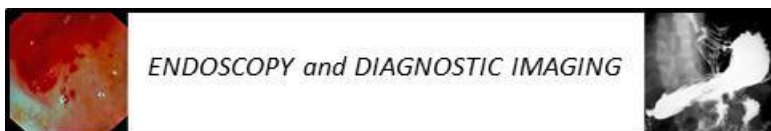
Pre and post fundo mechanical obstruction"pre-bolus obstruction pattern



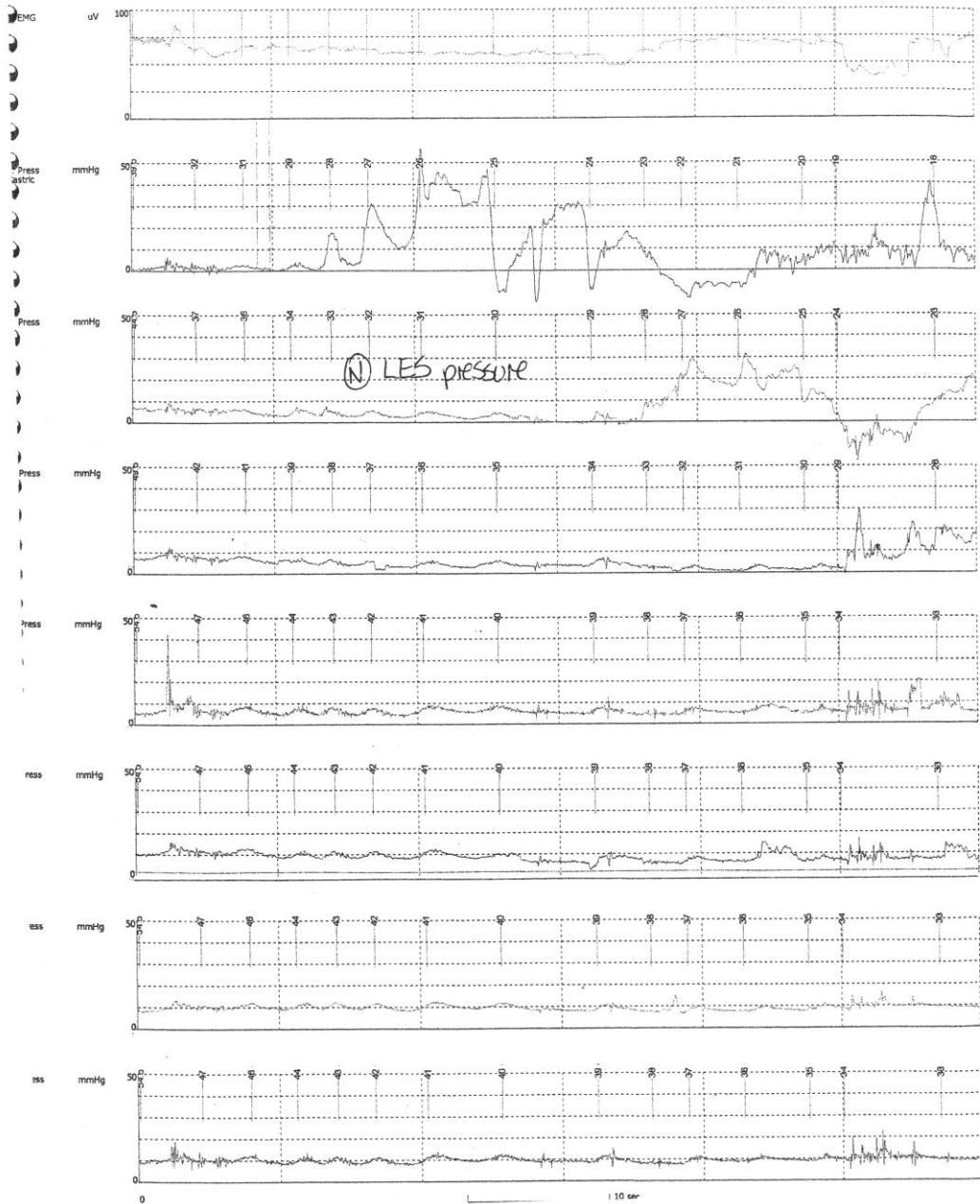
Channel Water Perfused Esophageal Manometry



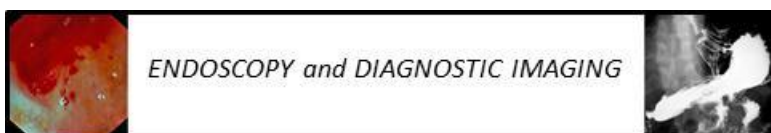
Pre and post fundus mechanical obstruction "pre-bolus obstruction pattern"



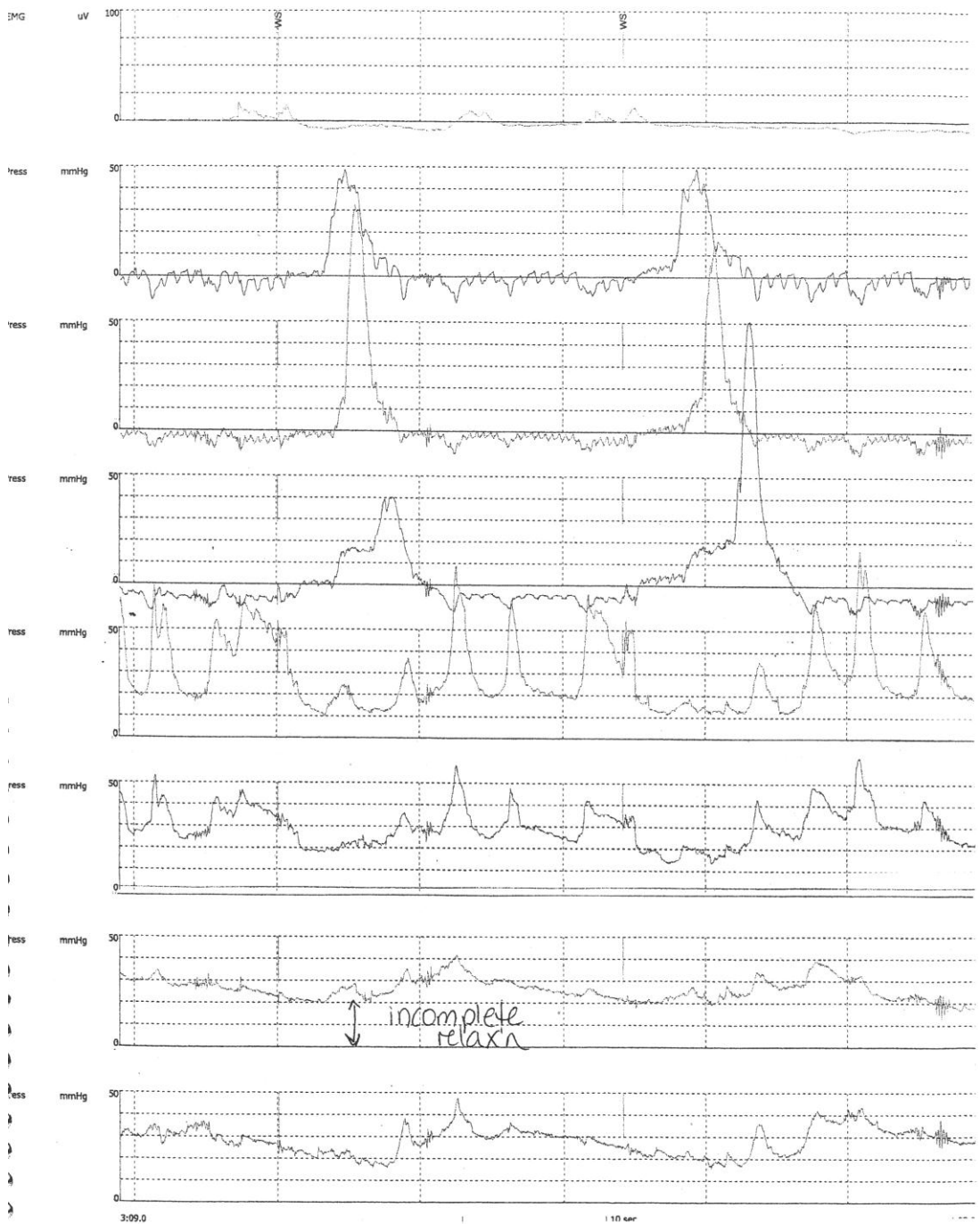
Channel Water Perfused Esophageal Manometry



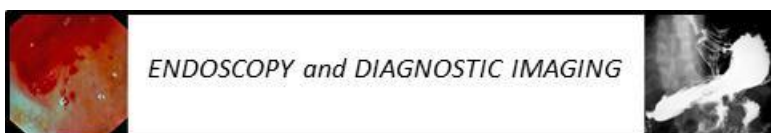
Pre and post fundus mechanical obstruction"pre-bolus obstruction pattern"



Channel Water Perfused Esophageal Manometry



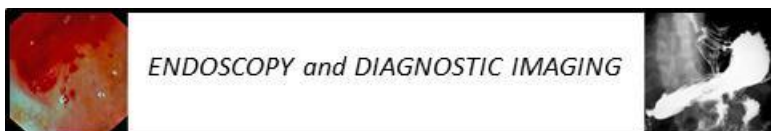
Pre and post fundus mechanical obstruction "pre-bolus obstruction pattern"



Channel Water Perfused Esophageal Manometry



Pre and post fundus mechanical obstruction "pre-bolus obstruction pattern"



Diffuse esophageal spasm

Clinical History:

Presenting Symptom: dysphagia

Other Symptom:

Lower esophageal sphincter (Normal values in brackets)

Resting pressure: 23 mm Hg
(16-30)

Relaxation duration: 13.3
seconds (>2)

% Relaxation: 92% (80-100%)

Residual Pressure: 3.3 mm Hg
(<8)

Esophageal body:

(Normal values in brackets)

Peristaltic contractions: 20% (>80%)

Simultaneous contractions: 80%
(<20%)

Mean contraction amplitude: 128 mm
Hg (30-180)

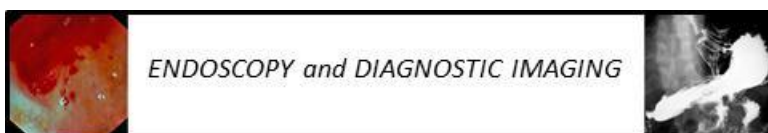
Mean contraction duration: 8.1 seconds
(<5.8)

Low amplitude contractions: 0% (<30%)

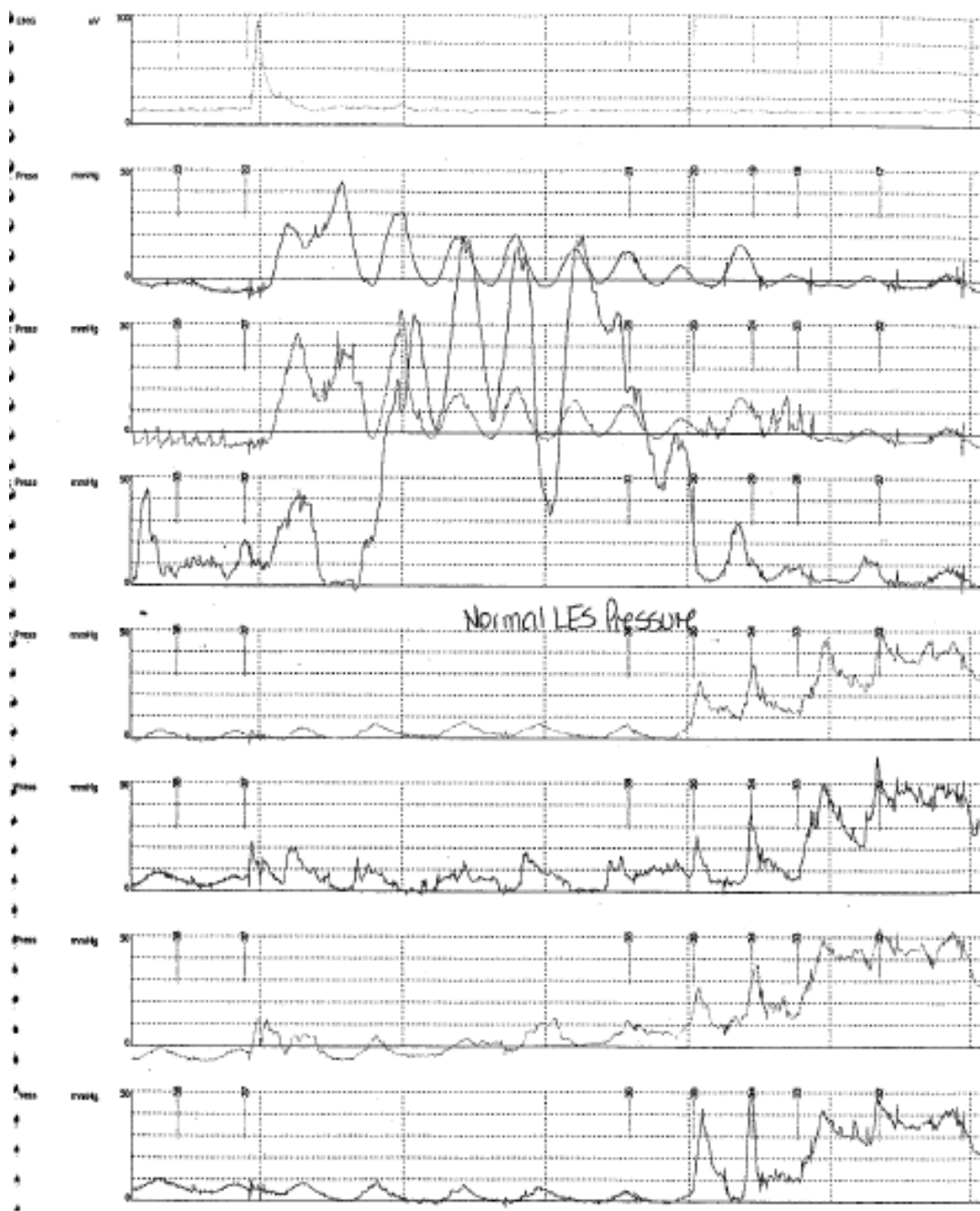
Spontaneous activity between
swallows: none

- **Acid Infusion Test:** not done
- **Pharyngo-Esophageal Sphincter (PE):** not done
 - Resting Pressure: 26.5 mm Hg (40-150)
 - Pharyngeal contraction pressure: 48.4 mm Hg (40-150)
 - Coordination: yes

Summary and Conclusions: Normal LES pressure. No evidence of esophageal retention. Marked motor abnormality body of esophagus. 80% of solicited swallows are simultaneous from mid to distal esophagus, and are of increased duration in distal esophagus. Feeble PE. Query diffuse esophageal spasm vs. evolving achalasia.

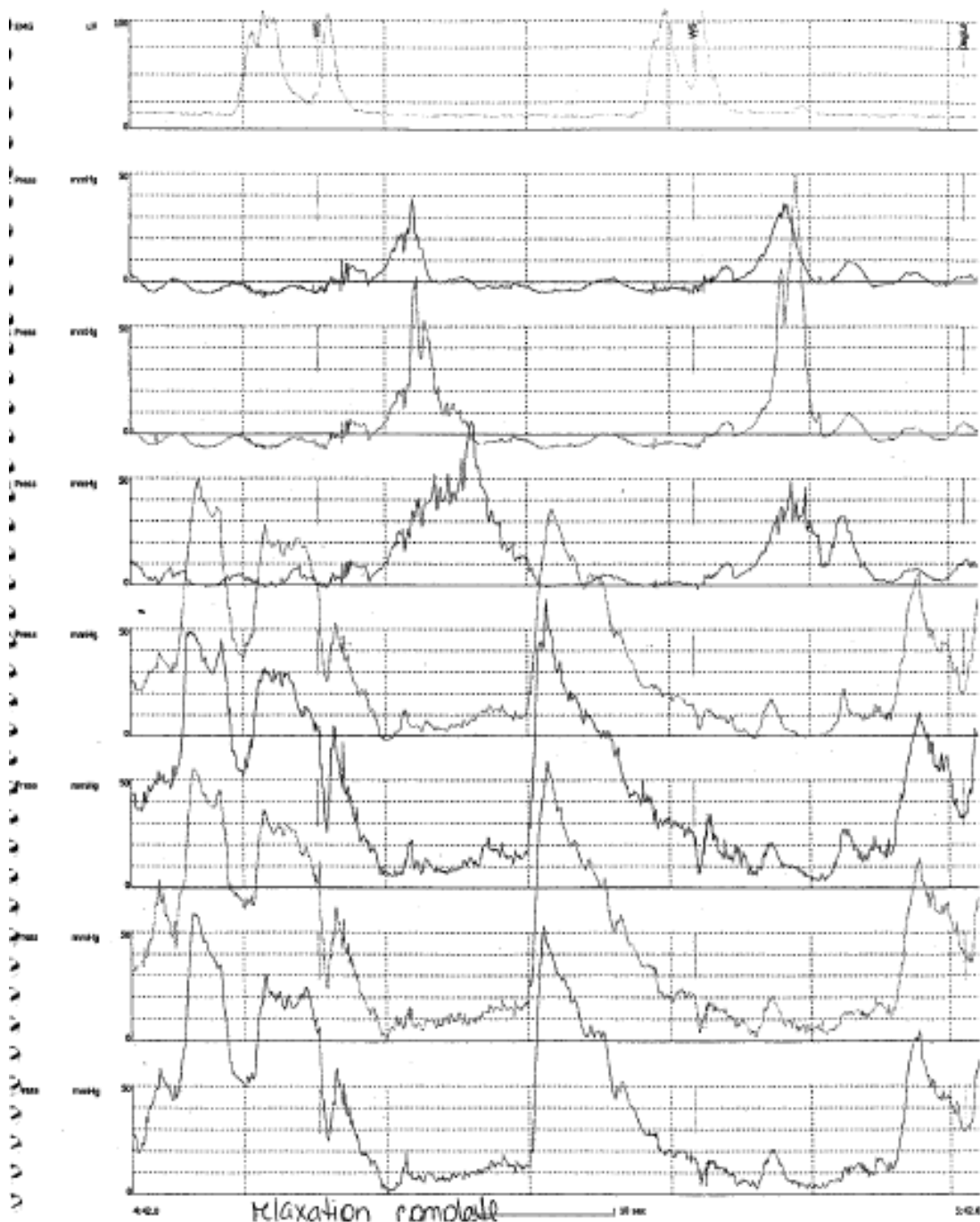


Channel Water Perfused Esophageal Manometry

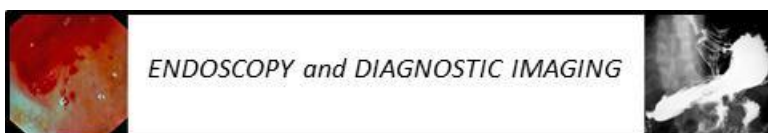


Diffuse esophageal spasm

Channel Water Perfused Esophageal Manometry



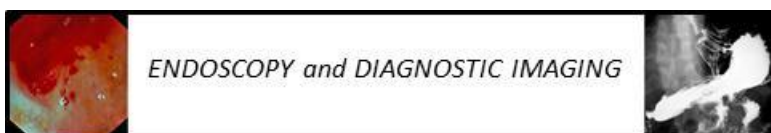
Diffuse Esophageal Spasm



Channel Water Perfused Esophageal Manometry



Diffuse Esophageal Spasm



Nutcracker esophagus

Clinical History:

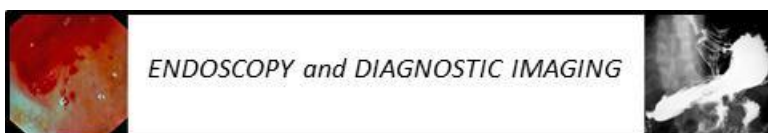
Presenting Symptom: heartburn

Other Symptom:

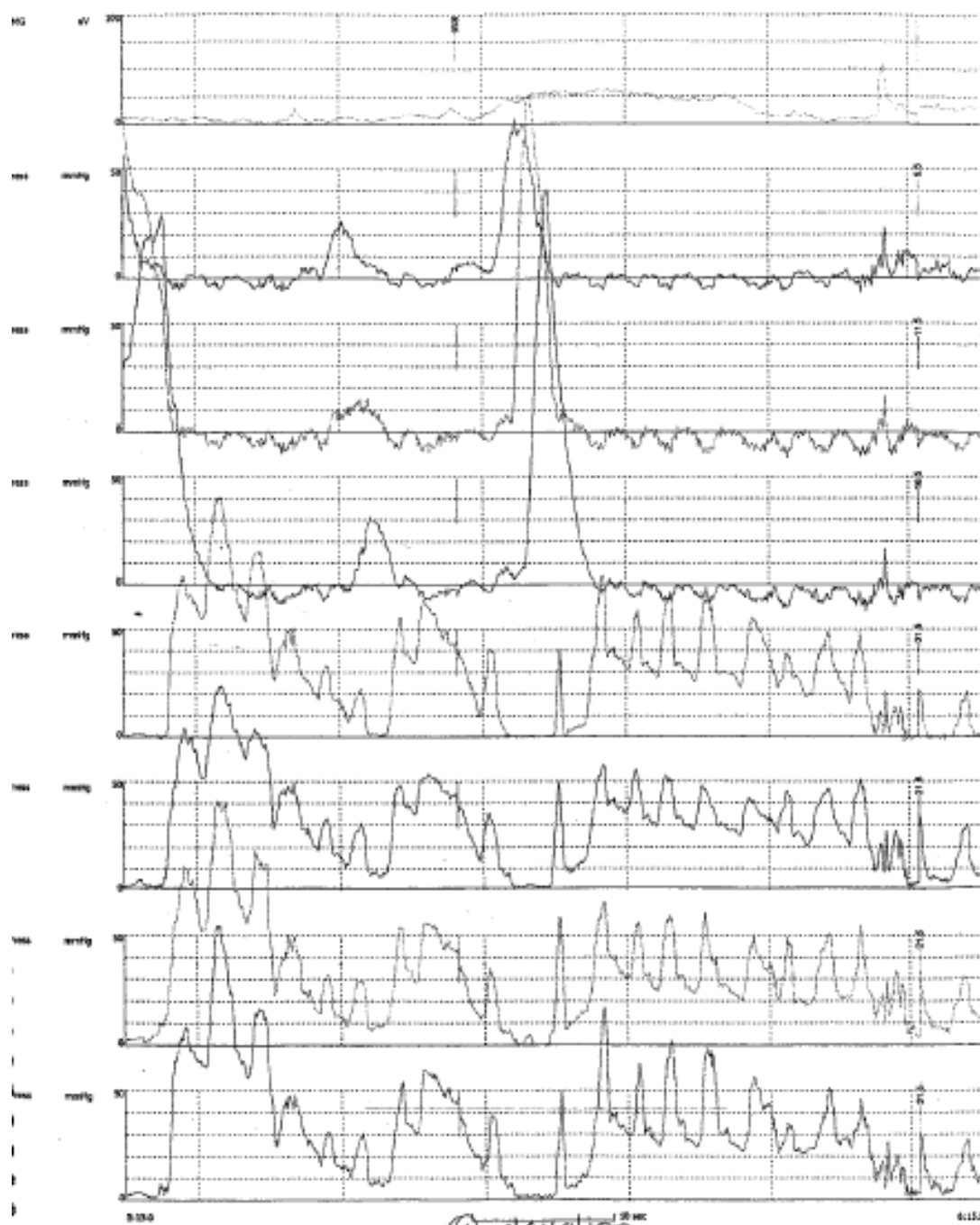
Lower esophageal sphincter (Normal values in brackets)	Esophageal body: (Normal values in brackets)
Resting pressure: 34 mm Hg (16-30)	Peristaltic contractions: 100% (>80%)
Relaxation duration: 10.3 seconds (>2)	Simultaneous contractions: 0% (<20%)
% Relaxation: 98% (80-100%)	Mean contraction amplitude: 241 mm Hg (30-180)
Residual Pressure: 0.5 mm Hg (<8)	Mean contraction duration: 6.1 seconds (<5.8)
	Low amplitude contractions: 0% (<30%)
	Spontaneous activity between swallows: none

- **Acid Infusion Test:** Felt pharyngeal burning by two minutes of infusion, which became stronger by three minutes and radiated to epigastric area. With water, all symptoms gone by six minutes.
- **Pharyngo-Esophageal Sphincter (PE):** Not done
 - Resting Pressure: mm Hg (40-150)
 - Pharyngeal contraction pressure: mm Hg (40-150)
 - Coordination:

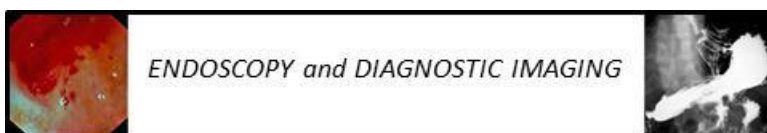
Summary and Conclusions: Hypertensive LES. Marked motor abnormality body of esophagus. Peristalsis present with all waves of increased amplitude and 60% of waves of increased duration. Positive acid infusion test – see text. Compatible with nutcracker esophagus.



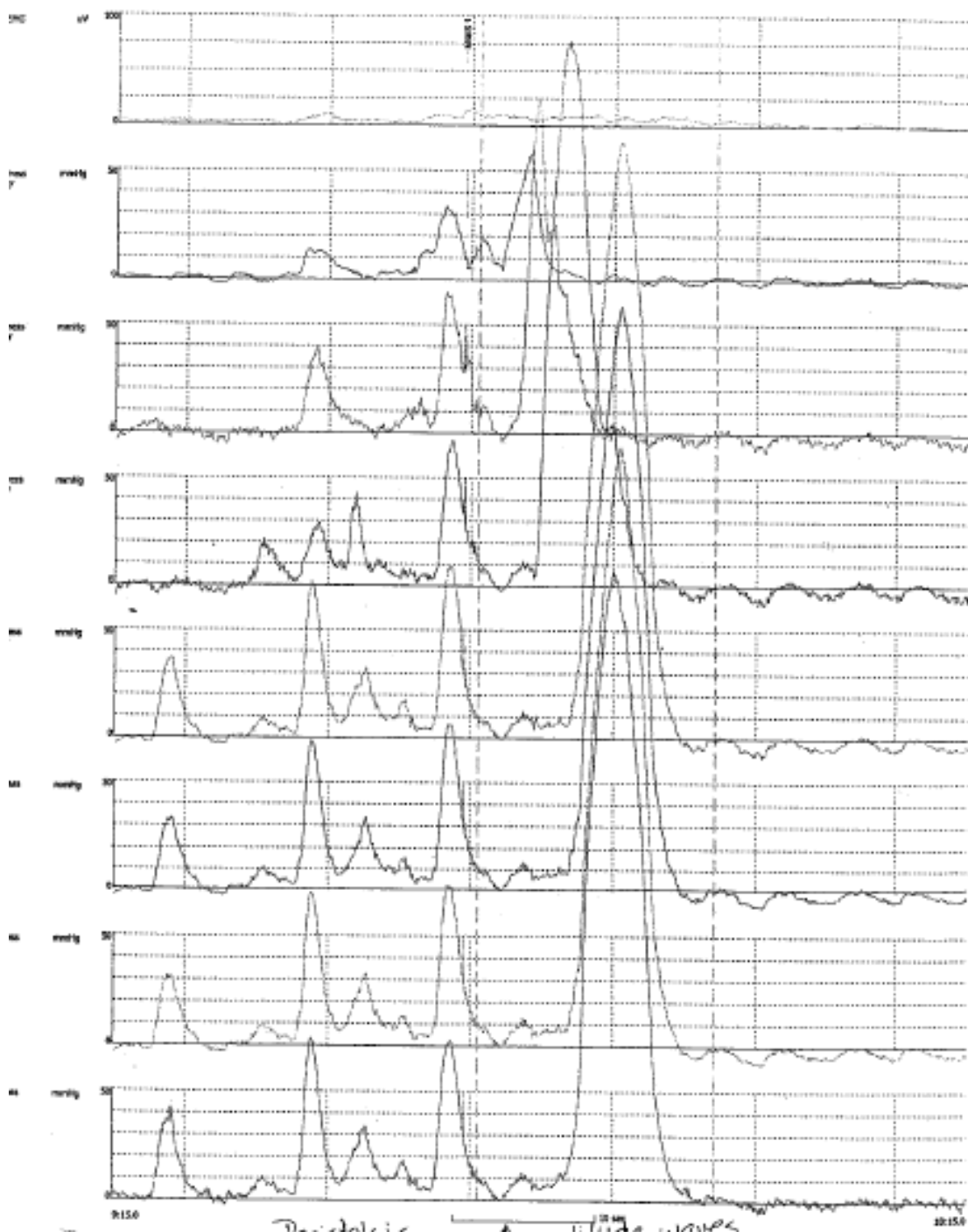
Channel Water Perfused Esophageal Manometry



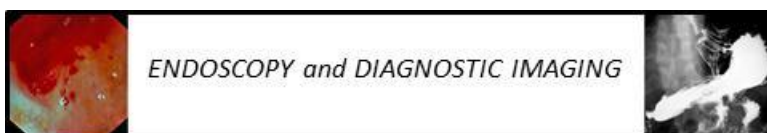
Nutcracker Esophagus



Channel Water Perfused Esophageal Manometry



Nutcracker Esophagus



Symptomatic wave with chest pain

Clinical History:

Presenting Symptom: dysphagia in chest

Other Symptoms: pain with dysphagia

Lower esophageal sphincter (Normal values in brackets)

Resting pressure: 26 mm Hg (16-30)

Relaxation duration: 16.9 seconds (>2)

% Relaxation: 96% (80-100%)

Residual Pressure: 1.2 mm Hg (<8)

Esophageal body: (Normal values in brackets)

Peristaltic contractions: 80% (>80%)

Simultaneous contractions: 20% (<20%)

Mean contraction amplitude: 96 mm Hg (30-180)

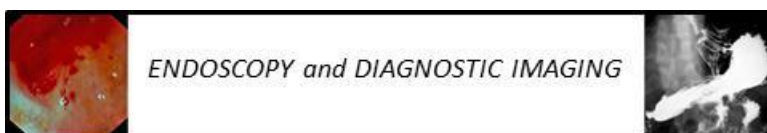
Mean contraction duration: 5.9seconds (<5.8)

Low amplitude contractions: 20% (<30%)

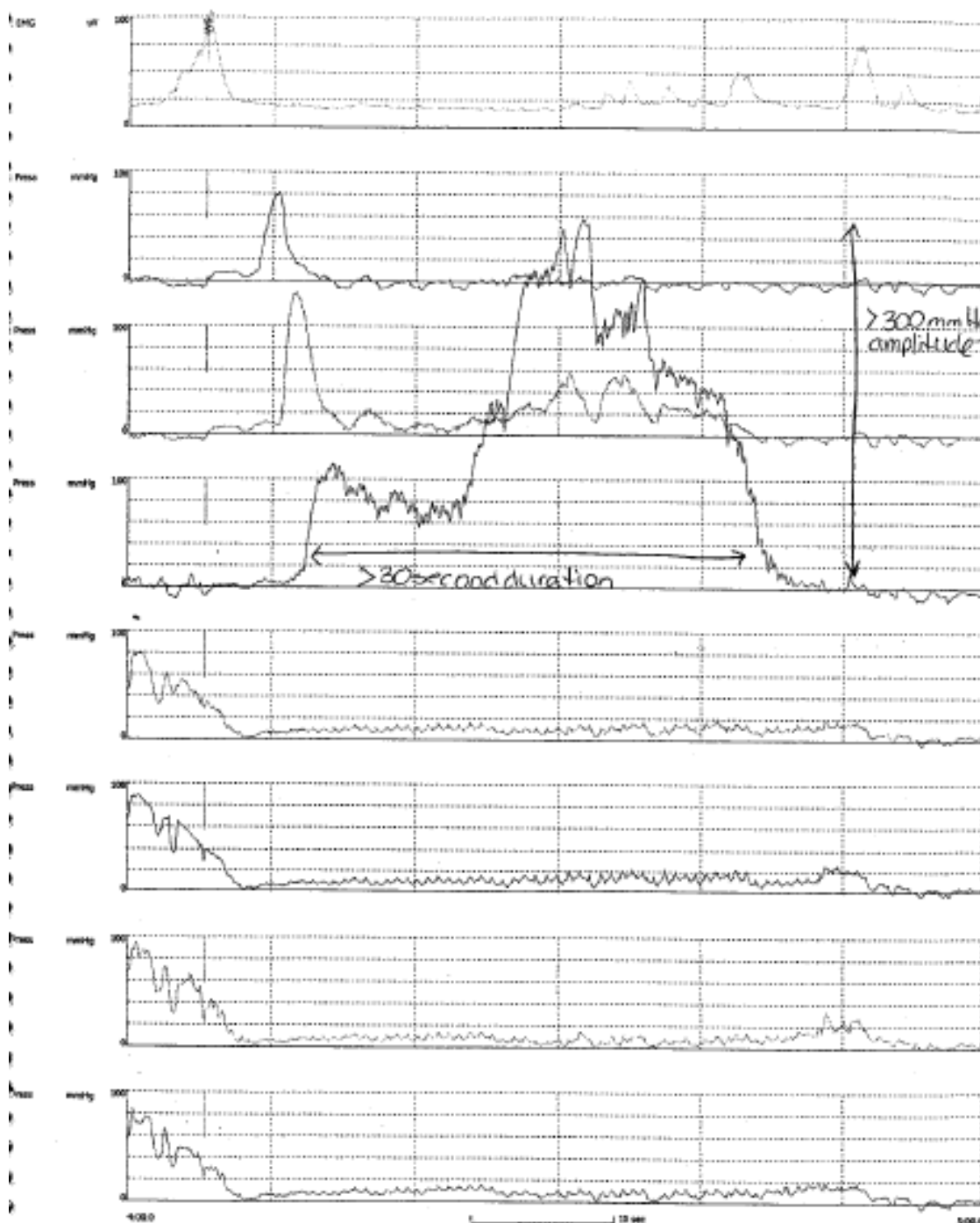
Spontaneous activity between swallows: none

- **Acid Infusion Test:** Not done
- **Pharyngo-Esophageal Sphincter (PE):** Not done
 - Resting Pressure: mm Hg (40-150)
 - Pharyngeal contraction pressure: mm Hg (40-150)
 - Coordination:

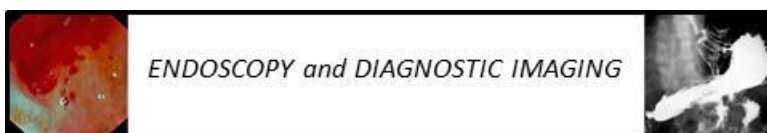
Summary and Conclusions: Normal LES pressure. Significant motor abnormality body of esophagus. Peristalsis present with 40% of waves of increased duration and symptomatic with pain. One incident noted during relaxation testing of shortness of breath while wave in lower esophageal body exceeding 300 mm Hg in amplitude, and 30 seconds duration.



Channel Water Perfused Esophageal Manometry



Symptomatic wave with chest pain



Scleroderma pattern

Clinical History:

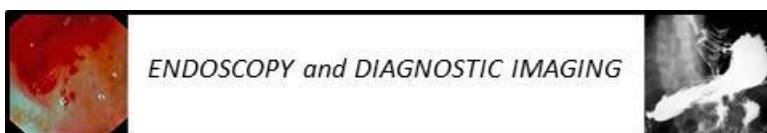
Presenting Symptom: chest pain

Other Symptoms: heartburn, regurgitation, dysphagia

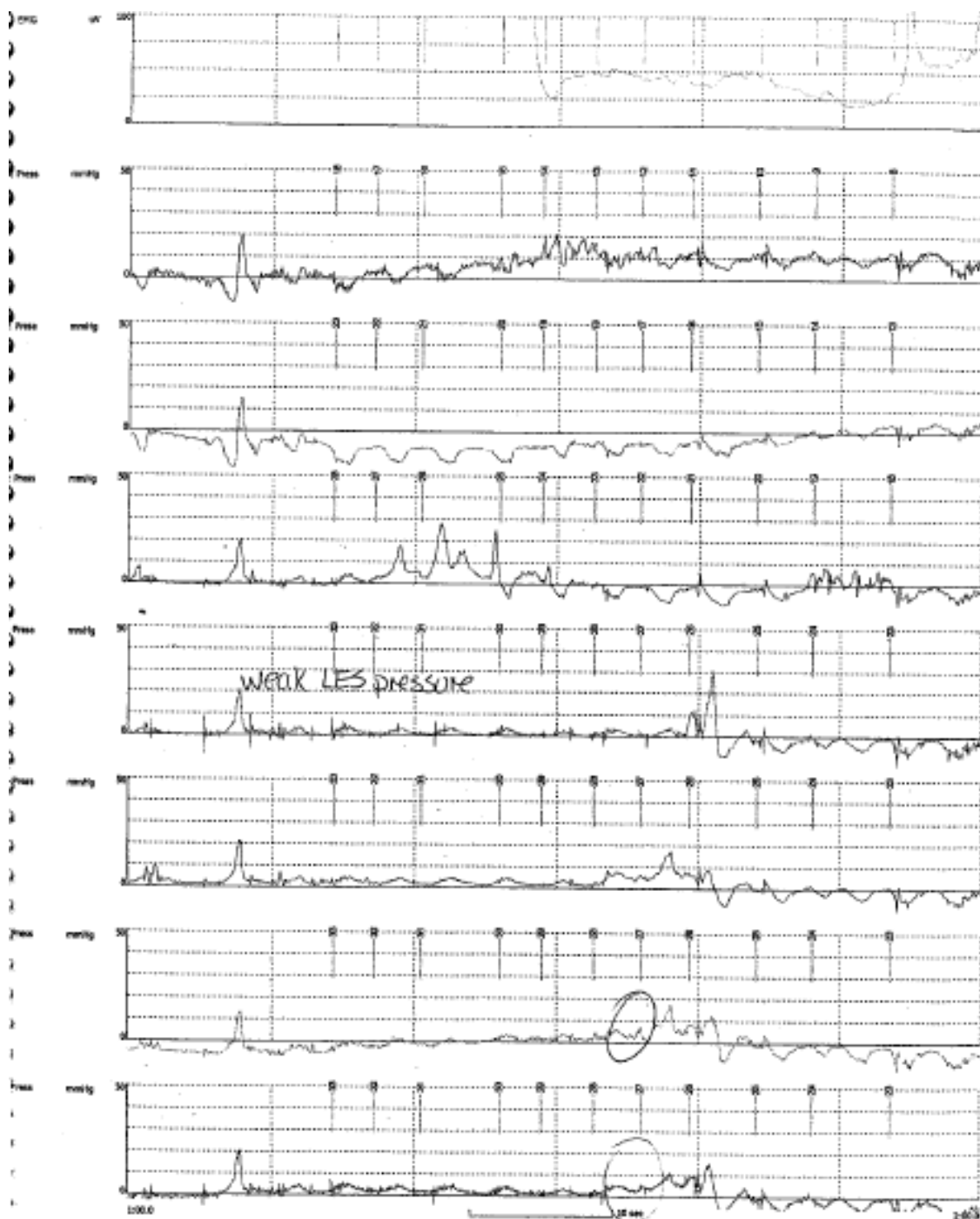
Lower esophageal sphincter (Normal values in brackets)	Esophageal body: (Normal values in brackets)
Resting pressure: 1 mm Hg (16-30)	Peristaltic contractions: 0% (>80%)
Relaxation duration: ? seconds (>2)	Simultaneous contractions: 0% (<20%)
% Relaxation: ? % (80-100%)	Mean contraction amplitude: ? mm Hg (30-180)
Residual Pressure: ? mm Hg (<8)	Mean contraction duration: ? seconds (<5.8)
<i>Difficult to assess relaxation due to low LES pressure</i>	Low amplitude contractions: 0% (<30%)
	Spontaneous activity between swallows: none

- **Acid Infusion Test:** not done
- **Pharyngo-Esophageal Sphincter (PE):**
 - Resting Pressure: 44.8 mm Hg (40-150)
 - Pharyngeal contraction pressure: 54.3 mm Hg (40-150)
 - Coordination: Yes

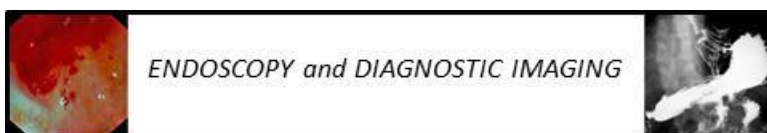
Summary and Conclusions: Feeble LES pressure. Marked motor abnormality body of esophagus. No peristalsis seen, all waves are non-conducted. Normal PE. Compatible with scleroderma pattern.



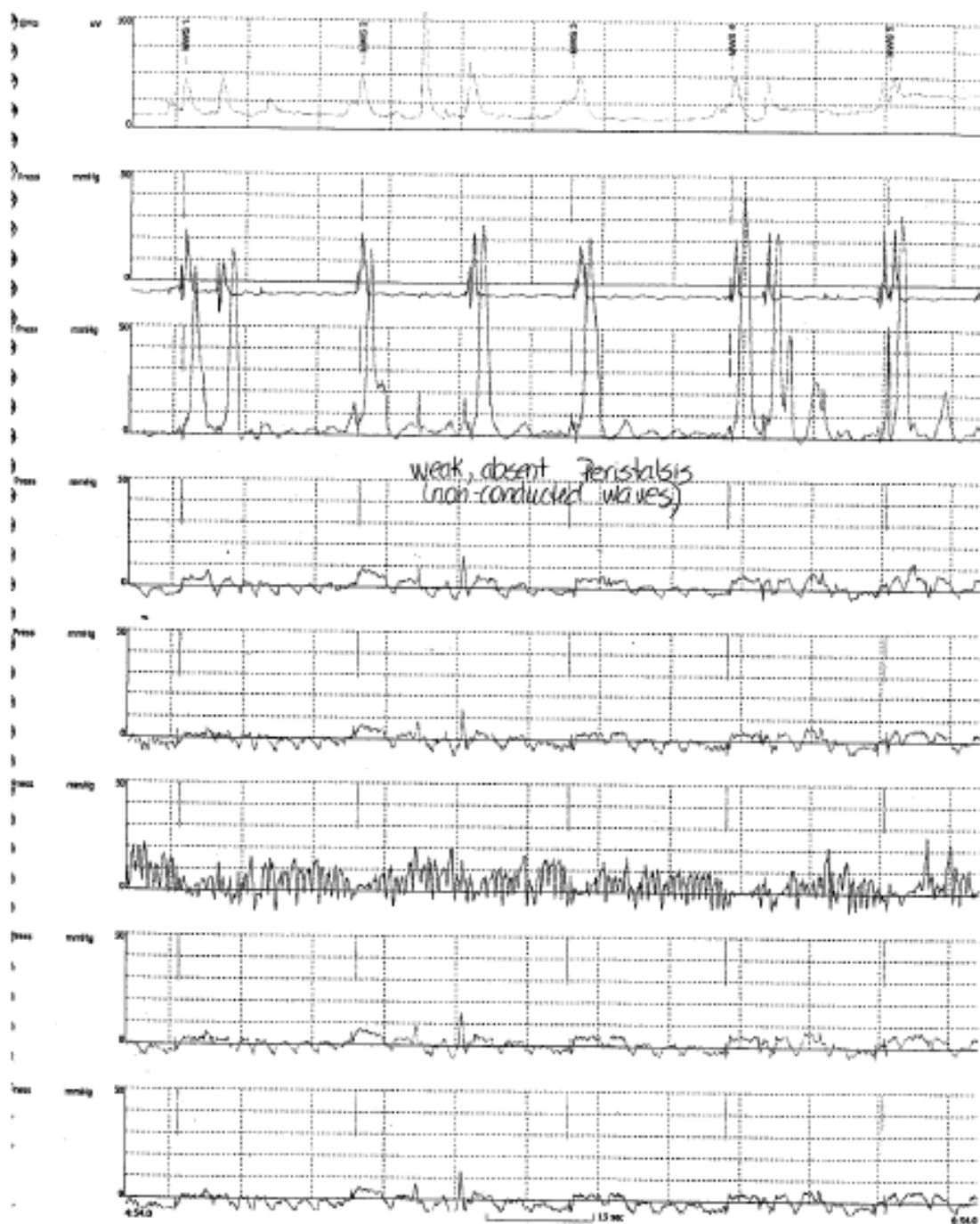
Channel Water Perfused Esophageal Manometry



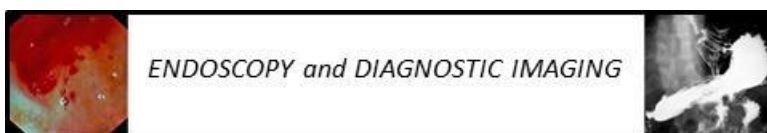
Scleroderma Pattery



Channel Water Perfused Esophageal Manometry



Scleroderma Pattern



Achalasia

Clinical History:

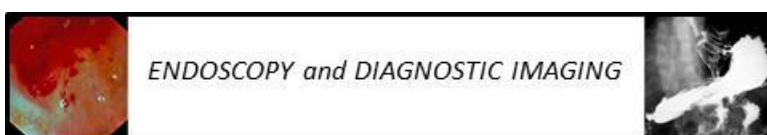
Presenting Symptom: dysphagia in chest

Other Symptoms: heartburn, regurgitation, chest pain, vomiting

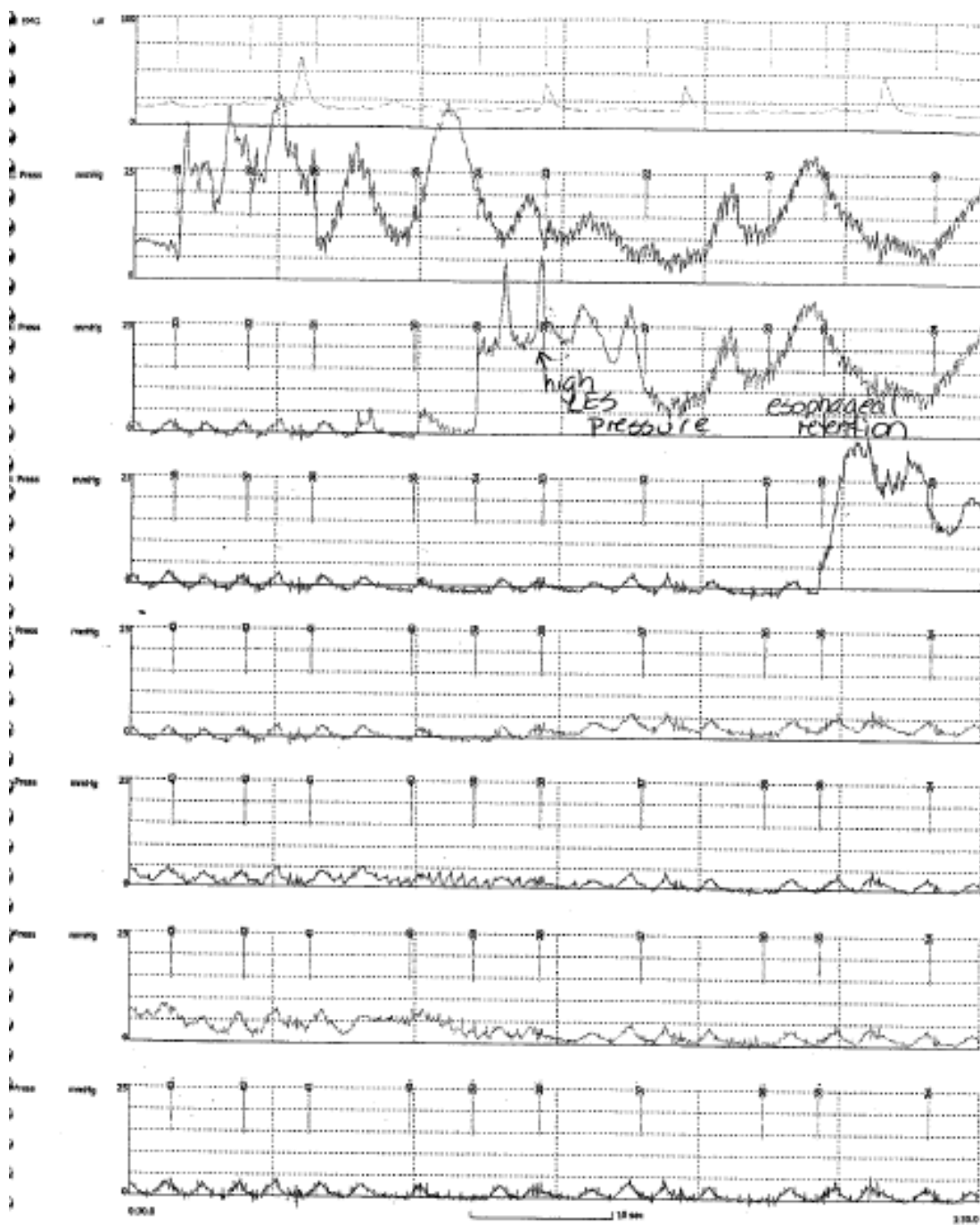
Lower esophageal sphincter (Normal values in brackets)	Esophageal body: (Normal values in brackets)
Resting pressure: 23 mm Hg (16-30)	Peristaltic contractions: 0% (>80%)
Relaxation duration: 6 seconds (>2)	Simultaneous contractions: 100% (<20%)
% Relaxation: 58.5% (80-100%)	Mean contraction amplitude: 16 mm Hg (30-180)
Residual Pressure: 9.3 mm Hg (<8)	Mean contraction duration: 2.7 seconds (<5.8)
	Low amplitude contractions: 100% (<30%)
	Spontaneous activity between swallows: none

- **Acid Infusion Test:** not done
- **Pharyngo-Esophageal Sphincter (PE):** not done
 - Resting Pressure: mm Hg (40-150)
 - Pharyngeal contraction pressure: mm Hg (40-150)
 - Coordination:

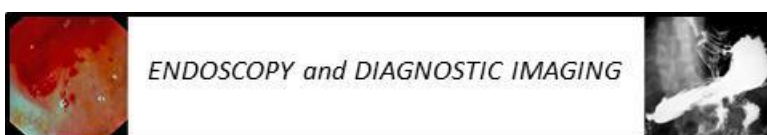
Summary and Conclusions: Normal LES pressure. Relaxations incomplete and esophageal retention evident. Marked motor abnormality body of esophagus. No peristalsis seen. All waves simultaneous and of decreased amplitude. Diagnostic of achalasia.



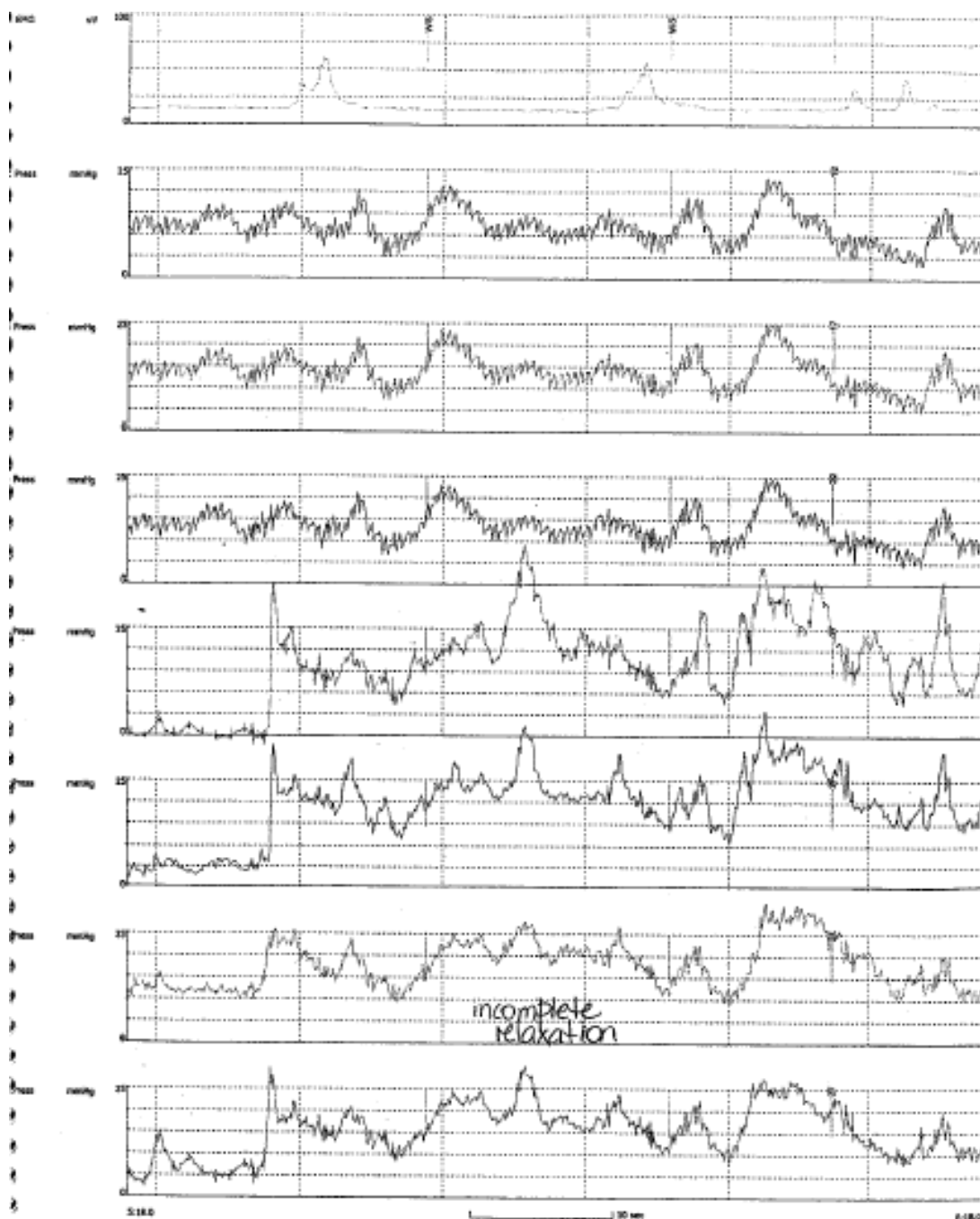
Channel Water Perfused Esophageal Manometry



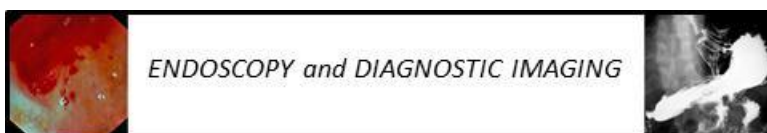
Achalasia



Channel Water Perfused Esophageal Manometry

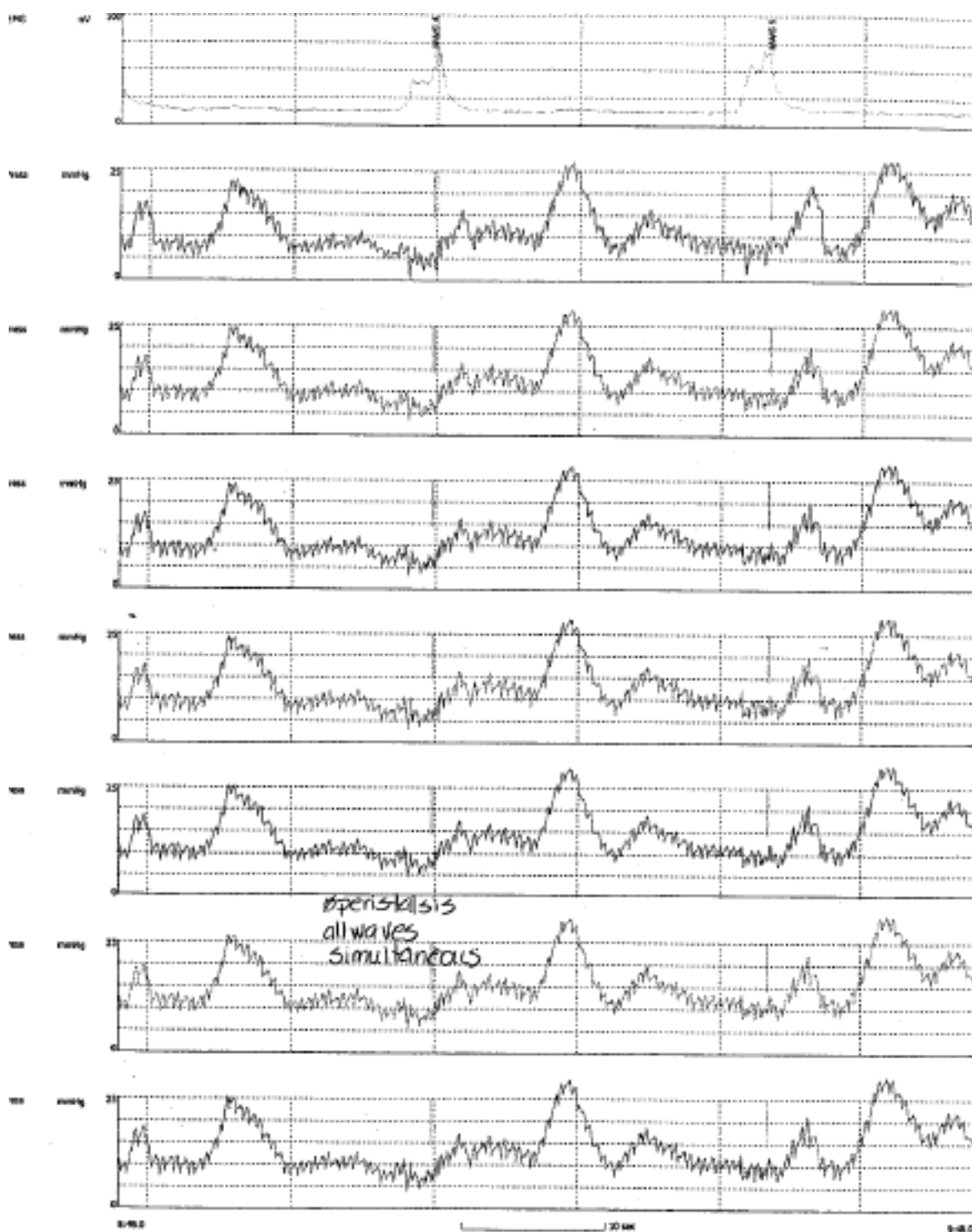


Achalasia

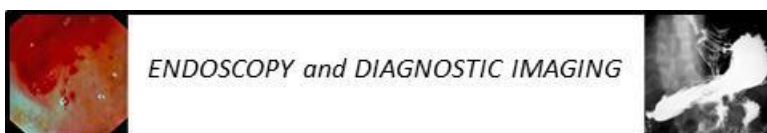


ENDOSCOPY and DIAGNOSTIC IMAGING

Channel Water Perfused Esophageal Manometry



Achalasia



Incoordinate PE

Clinical History:

Presenting Symptom: dysphagia

Other Symptom:

Lower esophageal sphincter (Normal values in brackets)

Resting pressure: 14 mm Hg
(16-30)

Relaxation duration: 11.6
seconds (>2)

% Relaxation: 97% (80-100%)

Residual Pressure: 0 mm Hg
(<8)

Esophageal body:

(Normal values in brackets)

Peristaltic contractions: 100%
(>80%)

Simultaneous contractions: 0%
(<20%)

Mean contraction amplitude: 49
mm Hg (30-180)

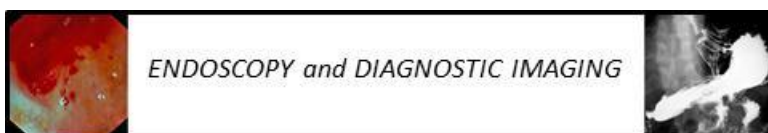
Mean contraction duration: 2.7
seconds (<5.8)

Low amplitude contractions: 0%
(<30%)

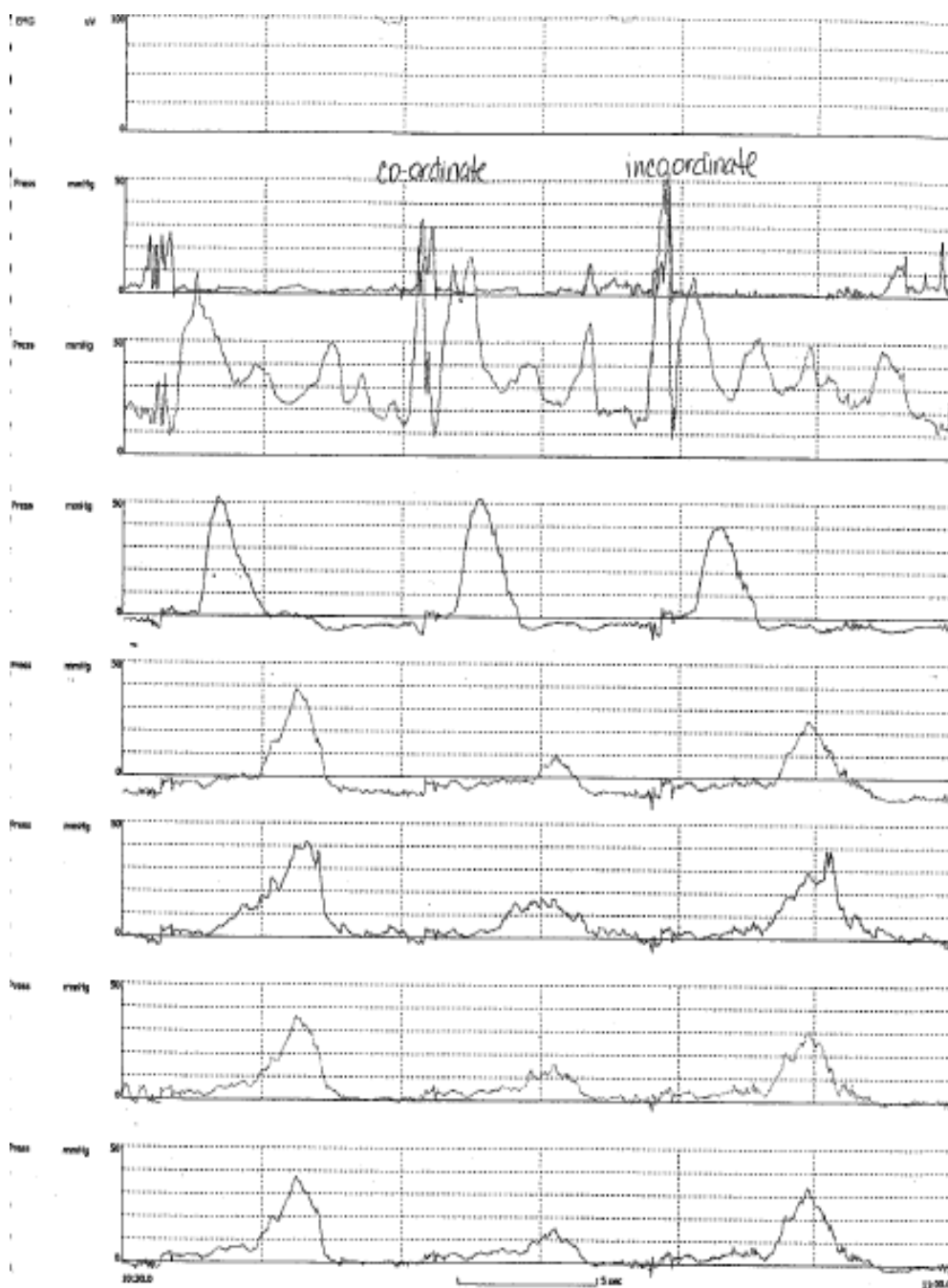
Spontaneous activity between
swallows: none

- **Acid Infusion Test:** not done
- **Pharyngo-Esophageal Sphincter (PE):** not done
 - Resting Pressure: 24 mm Hg (40-150)
 - Pharyngeal contraction pressure: 36 mm Hg (40-150)
 - Coordination: no

Summary and Conclusions: Feeble LES pressure. Normal body study. Peristalsis present. Feeble and incoordinate PE.

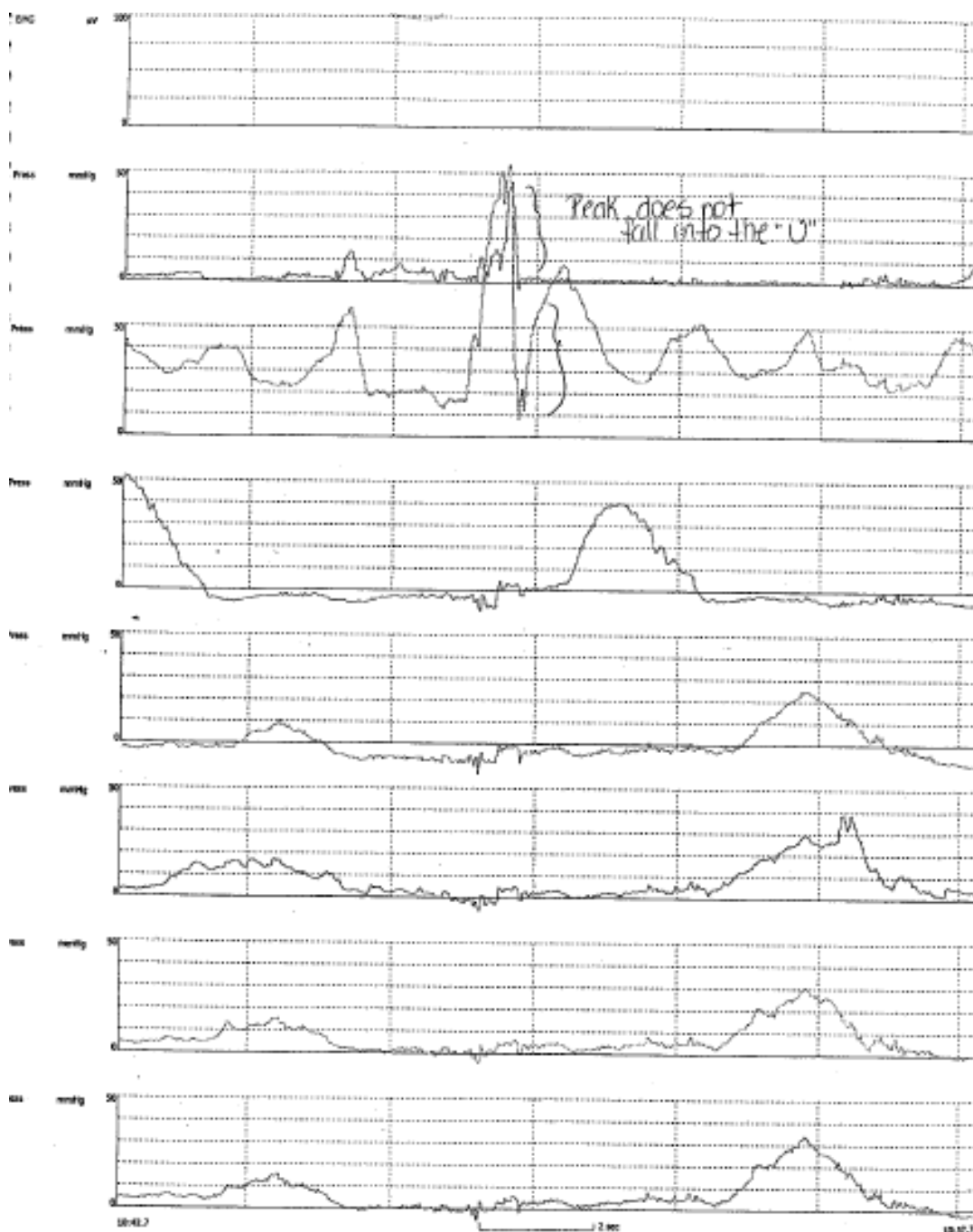


Channel Water Perfused Esophageal Manometry

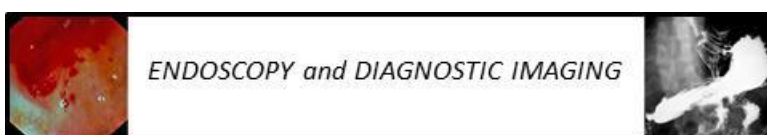


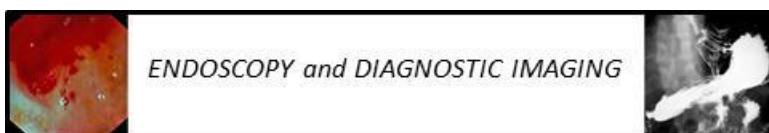
Inco-ordinate PE

Channel Water Perfused Esophageal Manometry



Inco-ordinate PE





STOMACH

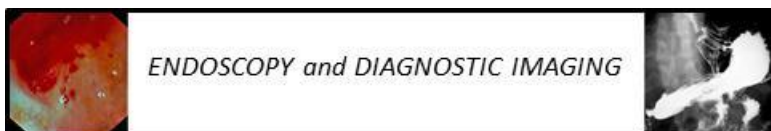
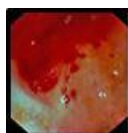


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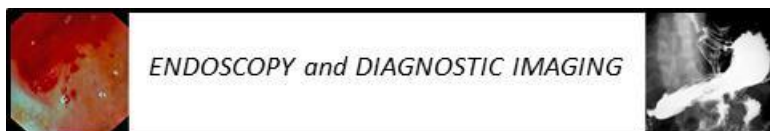


STOMACH

“Sharpening Knowledge to Enhance Clinical Skill”

GASTRIC SURGERY

- Bariatric procedures and complications.
 - Specific procedures
 - Gastric bypass (Roux-en-Y)
 - Anastomotic leak with peritonitis
 - Stomal stenosis
 - Marginal ulcers (ischemia)
 - Staple line disruption
 - Internal and incisional hernias
 - Nutrient deficiencies (usually iron, calcium, folic acid, vitamin B12)
 - Dumping syndrome
 - Gastroplasty
 - GERD
 - Stomal stenosis
 - Staple line disruption
 - Band erosion
 - Gastric banding
 - Band slippage
 - Erosion
 - Esophageal dilation
 - Band infections
 - Biliopancreatic diversion
 - Anastomotic leak with peritonitis
 - Protein-energy malnutrition
 - Vitamin and mineral deficiencies
 - Dehydration
 - Complications common to all bariatric surgical procedures
 - CNS
 - Psychiatric disturbance
 - Lung
 - Atelectasis and pneumonia
 - Deep vein thrombosis
 - Pulmonary embolism
 - CVS
 - GI
 - Anemia
 - Diarrhea
 - Ulceration



- GI bleeding
- Stenosis
- Gallstone
- o Metabolic
 - Bone disease
 - Too rapid weight loss
- o Surgical
 - Wound infection
 - Failure to lose weight
 - Mortality (0.5-1%)

Abbreviation: CNS, central nervous system

Adapted from: Klein S. *2006 AGA Institute Post Graduate Course*: pg. 175.

- Mechanisms or causes of iron- and B12-deficiency associated anemia, diarrhea, metabolic bone disease, and recurrent gastric ulceration in a patient having had a Billroth II partial gastrectomy for peptic ulcer disease (PUD), gastric cancer (GCA) or morbid obesity (bariatric surgery) for increased BMI.

➤ Iron

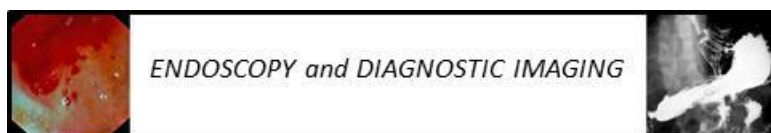
- o Pre-surgery iron deficiency
- o Decreased intake from post-op symptoms (anorexia, early satiety)
- o Decreased acid leads to decreased pepsin and decreased meat (iron) digestion
- o Decreased acid: inhibits the acid-mediated solubilizing and reducing of inorganic dietary iron (Fe^{3+} [ferric] .. Fe^{2+} ferrous)]
- o Decreased absorption of Fe^{2+} , Ca^{2+} , B12, bypassing site of maximal absorption
- o Can be slow bleeding at surgical site
- o Bile gastritis
- o Gastric stump cancer

➤ B12

- o Pre-surgery deficiency
- o Decreased intake
- o Loss of stimulated co-ordinated release of pancreatic “R” factor
- o Decreased intrinsic factor
- o Loss of HCl/pepsinogen to liberate food B12
- o Bacterial overgrowth syndrome

➤ Diarrhea

- o Magnesium-containing antacids, PPI's

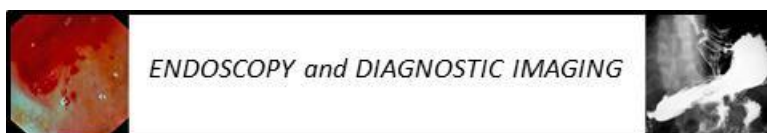


- Dumping
 - Retained antrum (↑ gastrin)
 - Hypergastrinemia, HCL hypersecretion (↑ volume, mucosal damage)
 - Bypassed duodenum
 - Unmasked celiac disease
 - Unmasked lactose intolerance
 - Unmasked bile acid wastage
 - Primary or secondary (unmasked) pancreatic insufficiency
 - Small Intestinal bacterial overgrowth (SIBO)
- Metabolic bone disease
- Pre-existing osteoporosis ↓ Ca^{2+} solubilization
 - ↓ vitamin D or Ca^{2+} intake
 - Bypass of site of maximal absorption of Ca^{2+} (duodenum)
 - Binding Ca^{+2} (unabsorbed fatty acids)
- Peptic ulceration (previous peptic ulcer disease [PUD])
- ↑ gastrin – ZES, incomplete vagotomy, gastric retention, afferent loop syndrome
 - H. pylori infection
 - NSAIDs, ASA use
 - “Stump” Cancer
 - Ischemia at anastomosis
 - Bile gastritis
- Presentations of ZES (Zollinger Ellison Syndrome)
- PUD – severe, multiple, unusual sites
 - Diarrhea
 - Recurrent ulceration (with or without gastric surgery)
 - Associated MEN I syndrome
 - Thick gastric folds

Abbreviations: SIBO, small intestinal bacterial overgrowth; GCa, gastric cancer; MEN, multiple endocrine neoplasia ; PPIs, proton pump inhibitor; PUD, peptic ulcer disease; ZES, Zollinger-Ellison syndrome

- The presenting features of ZES, and their approximate frequency

- Presenting features of ZES
- Abdominal pain (75%-100%)
 - Diarrhea (35%--73%) (isolated in up to 35%)
 - Pain and diarrhea (55%-60%)
 - Heartburn (44%-64%)
 - Duodenal (and prepyloric) ulcers (71%-91%)
 - Multiple ulcers in unusual places



- Stomal ulcers
- PUD refractory to treatment
- Ulcer complications (bleeding, 1%-17%; perforation, 0%-5%, or obstruction, 0%-5%)
- With MEN1 (22%-24%)

Abbreviations: MEN, multiple endocrine neoplasia; PUD, peptic ulcer disease; ZES, Zollinger-Ellison syndrome

Adapted from: Metz DC, and Jensen RT. *Gastroenterology* 2008;135: pg. 1469-149.

Diagnostic imaging

- Post- gastric surgery
 - Fundoplication
 - Billroth I/II
 - Roux – en – Y
 - Stomal ulcer / cancer
 - Blown duodenal stump
 - Bile (reflux) gastritis
 - Jejuno gastric intussusceptions
 - Gastric remnant bezoar
- Stomal (marginal) ulcer
 - Usually within 2 cm of the stoma, the efferent limb of the jejunum after a gastroenterostomy
 - Finding include
 - Ulcer crater
 - Giant ulcer
 - Thick jejunal folds
 - Rigid efferent limbs
 - May develop jejunocolic fistula
- Afferent loop syndrome
 - Dilation of afferent limbs may have nonfilling of afferent limbs
 - Destruction of afferent limb after Billroth II anastomosis
 - Obstruction due to
 - Recurrent ulcer / tumor
 - Adhesions
 - Intend herniation
- Jejuno gastric intussusceptions
 - Tubular filling defect in gastric remnant after gastroenterostomy
 - Valvulae conniventes in tubular structure, representing efferent of afferent loop



- Stomal cancer (AKA stump carcinoma, post gastrectomy carcinoma)
 - Lobulated mass in gastric remnant (filling defect)
 - Mass may
 - Obstruct outlet of stomach
 - Produce mass effect on transverse colon
- Bile reflux gastritis
 - Filling defect in gastric remnant
 - Thick (edematous) gastric folds
 - Narrowing / deformity of gastric remnant and perianastomotic jejunum
- Thickened Folds
 - Zollinger – Ellison syndrome
 - Single / multiple ulcers in usual / unusual sites
 - Thick gastric folds
 - Fundic gland polyps
 - CT thick walls of stomach / duodenum may be pancreatic mass
 - Differential
 - Lymphoma
 - Nodular, irregular, thick folds variable size
 - Adenocarcinoma mass
 - Ménétrier disease
 - Proximal stomach
 - Thick gastric folds
 - Usually proximal half of stomach
 - Especially greater curve
 - Pliable (stomach can be distended)

GASTRIC DISMOTILITY: Gastroparesis

Practice Pointers: Gastroparesis

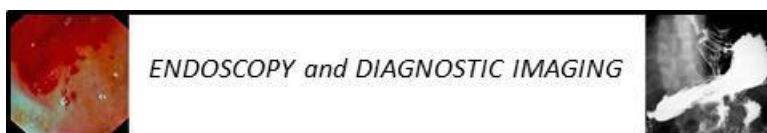
- The vomiting center is on the blood side of the blood-brain barrier
- Some persons with severe, intractable gastroparesis, such as may occur with severe type I diabetes, may improve with near-total gastrectomy and Roux-en-Y anastomosis
- Slowed gastric emptying and delayed small intestinal transit occur in persons with cirrhosis.
 - The assessment of gastric emptying includes measurement of emptying, accommodation and contractility (Smout and Mundt 2009, Szarka and Camilleri 2009).



- Accommodation of the proximal stomach is activated by vagally mediated relation.
 - There is no cephalic phase, but the accommodation reflex is imitated in the cropharynx, stomach and duodenum (Vanden Berghe et al. 2009).
 - If the pylorus is obstructed and food does not enter the duodenum, the amplitude of the accommodation reflex will be less and the person will feel full.
 - The symptoms of gastroparesis may be troublesome, but curiously there is not a good association between measures of gastric emptying and severity of symptoms.
 - The physical subscore of the Short-Form I2 as a measure of quality of life, and the Hospital Anxiety and Depression Scale correlated with gastroparesis severity as measured by the Gastroparesis Cardinal Symptom Index, and did not correlate with gastric emptying delay or symptom duration (Bielefeldt et al. 2009).
- The smooth muscle mechanism (s) of action of 6 prokinetic drugs used for the treatment of symptoms of gastroparesis (see question 11), and indicate the FDA pregnancy use category of those that may be caused during pregnancy.
 - Metoclopramide (FDA B)
 - Central/peripheral dopamine receptor antagonist (D_2)
 - 5-HT₃ receptor antagonist
 - 5-HT₄ receptor agonist
 - Domperidone (FDA C)
 - peripheral D_2 antagonist
 - Cisapride (FDA C)
 - muscarinic (acetylcholine) receptor agonist
 - 5-HT₃ receptor antagonist
 - 5-HT₄ receptor agonist
 - Ondansatron (FDA B)
 - 5-HT₃ receptor antagonist
 - Erythromycin (FDA B)
 - motilin receptor agonist
 - Tegaserod
 - Cholinergic 5-HT₄ partial agonist
 - Bethanechol
 - muscarinic receptor agonist
 - Anticholinergic (buscopan, for tachygastria)
 - α -adrenergic antagonists
 - α -adrenergic antagonist
 - Botulism toxin injections
 - phosphodiesterase inhibitors (Viagra)
 - Octreotide injections
 - somatostatin receptor antagonist

*The FDA category for use in pregnancy is noted in brackets

Adapted from: Quigley EMM. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1007.



- Therapeutic options for the treatment of nausea and vomiting during pregnancy, including dietary and lifestyle modifications, and medical therapy.

➤ Dietary and lifestyle modifications

- Avoidance of precipitating factors
- Frequent, small meals high in carbohydrate and low in fat
- Stimulation of P6 acupuncture point
- Ginger
- Vitamin B6

Printed with permission : Keller J, et al. *Nature Clinical Practice Gastroenterology & Hepatology* 2008; 5(8): pg. 433.

- The mechanisms, risk factors and methods to reduce PONV (post-operative nausea & vomiting) (early PONV, 0-2 hour post-op; late PONV, 2-24 hours post-op).

➤ Mechanism

- Release of serotonin from bowel handling that stimulates 5HT₃ receptors on afferent serotonergic pathways that stimulate the brainstem
- Reduced blood flow to brainstem during surgery
- Activated cerebral cortical pathways

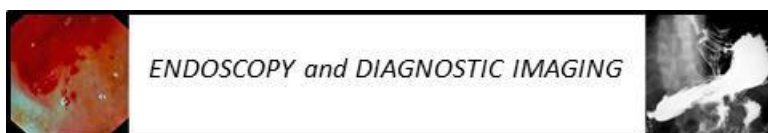
➤ Risk factors for PONV

- Post Puberty females
- Non-smokers
- Previous PONV
- Use of volatile anesthetics
- Intra-operative use of opiates
- High dose neostigmine
- Prolonged surgery
- Intra-abdominal surgery
- Major gynecological surgery

➤ Methods to reduce the risk of PONV

- Avoid opioids
- Avoid nitrous oxide
- Avoid high-dose reversal agent
- Adequate hydration
- High oxygen concentration
- Propofol anesthetic

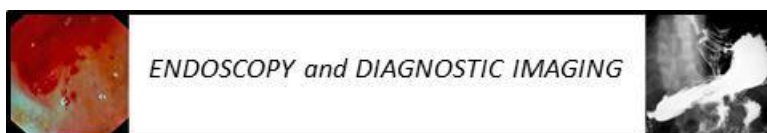
Abbreviation: PONV, post-operative nausea & vomiting



Printed with permission: Gan TJ, et al. *Anesth Analg* 2003;97(1):62-71.; and Williams KS. *Surg Clin North Am* 2005;85(6):1229-41.; and adapted from: Kovac AL. *J Clin Anesth* 2006 Jun;18(4):304-18.

- The differential diagnosis of vomiting in a newborn.
 - Gastroenteritis
 - Gastroesophageal reflux
 - Overfeeding
 - Food allergy
 - Milk protein intolerance
 - Congenital duodenal atresia
 - Pyloric stenosis
 - Volvulus
 - Meconium ileus
 - Hirschsprung's disease
- The non-pharmaceutical maneuvers that may be used to speed the rate of gastric emptying and be potentially useful for the treatment of the patient with gastroparesis.
 - Meal Factors
 - Small, frequent, fluid, neutral pH and temperature, isotonic, low energy density, low fat meals
 - Certain amino acids (e.g. L-tryptophan – [cheese])
 - Avoid offending foods and beverages
 - Treat other factors
 - Underlying disease/ condition causing/ aggravating gastroparesis
 - Rectal/colonic distention
 - Pregnancy
 - Ascites
 - Hyperglycemia
 - Avoid circular vectoral motion
 - Avoid medications which may relax smooth muscle and thereby aggravate gastroparesis
 - Gastric electrical stimulation
 - Treat complications
 - Dehydration, electrolyte disturbances
 - Malnutrition

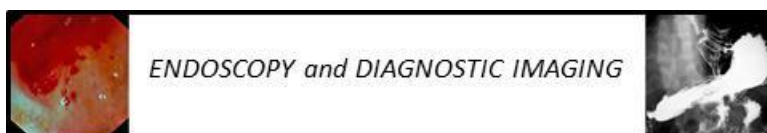
Adapted from: Quigley EMM. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1007.



- The non-pharmaceutical maneuvers that may be used to treat the patient with intractable nausea/vomiting.
 - Miscellaneous
 - Acupuncture – P6 acupuncture point
 - Gastric electrical stimulation
 - Treat the underlying cause
 - Treat the complications
 - Nutritional
 - Dehydration, electrolyte disturbances
 - Malnutrition
 - Vitamin B6 (thiamine) (FDA A)
 - Ginger
 - Soda crackers (unproven benefit)
 - Avoid offending foods/beverages
 - Frequent, small meals, low in fat
- The smooth muscle as well as the CNS receptors which are responsible for the mechanism (s) of action for 12 drugs used for the treatment of refractory nausea and vomiting, give one example of each, and indicate the FDA category for those that may be used during pregnancy.
 - GI receptors
 - Central
 - H-1 receptor antagonists – diphenhydramine, promethazine
 - Cannabinoids – dronabinol, nabilone
 - Neurokinin (NK)-1-antagonist – aprepitant, talnetant, osanetant
 - Neuroleptic – chlorpromazine, haloperidol
 - Benzodiazepines
 - Ondansatron – 5 HT3 antagonist
 - Tricyclic antidepressants
 - Steroids (e.g. dexamethasone) (FDA C), Mannitol (nausea and vomiting due to increased intracranial pressure)

Useful background: the “Dumping Syndrome”

- A frequent complication of esophageal, gastric or bariatric surgery.
- The early postprandial phase results from the rapid emptying of the stomach including larger than normal food particles, with the



osmotic shift of fluid into the duodenal lumen plus the distension of the human releasing gastrointestinal and pancreatic hormones.

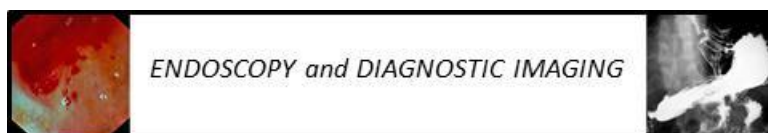
- This results in the gastrointestinal and vascular symptoms.
- The rapid and early absorption of nutrients causes prompt secretion of insulin, and the late dumping syndrome characterized by reactive hypoglycemia (Tack et al. 2009).
- A modified oral glucose tolerance test may be used to establish the reactive hypoglycaemia. The dumping syndrome does not always respond to dietary maneuvers, and pectin or guar gum may be needed to slow gastric emptying, a carbose to slow starch digestion and reduce pos-prandial reactive hypoglycaemia, or in extreme cases somatostatin injections may be given to slow gastric emptying and to slow sugar absorption.
- The drugs that may be used for nausea and vomiting in pregnancy and hyperemesis gravidarum during pregnancy, and give the FDA pregnancy use category.

Drug	FDA category
○ Vitamin B ₆	A
○ Doxylamine	B
○ Erythromycin (FDA category B; rarely used to treat hyperemesis)	Erythromycin (FDA category B; used rarely to treat hyperemesis)
○ Prochlorperazine	C
○ Metoclopramide	B
○ Ondansetron	B
○ Promethazine	C
○ Domperidone	C

Adapted from: Thukral C, and Wolf JL. *Nature Clinical Practice Gastroenterology & Hepatology* 2006; 3(5): pg. 258; and printed with permission: Keller J, et al. *Nature Clinical Practice Gastroenterology & Hepatology* 2008; 5(8): pg. 433.

Hypergastrinemia

- The investigation of the patient with confirmed fasting hypergastrinemia, performed after a detailed history and physical examination.
- Laboratory tests

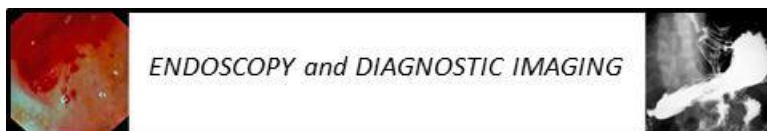


- Confirm fasting state from gastrin measurement
- Creatinine, calcium, PTH
- Chromogranin A (exclude renal failure)
- Schillings test, serum B₁₂
- Secretin infusion (increases paradoxically in ZES)
- TSN
- Urinary metanephrens
- Serum gastrin concentration
- Ca⁺² infusion (G↑↑)
- Basal and pentagastrin stimulated acid secretion (↑↑ BAO), BAO/MAO>60% (ZES)
- Food-stimulated acid secretin (G-cell hyperplasia/ hyperfunction)
- Endoscopy
 - EGD
 - Multiple ulcers in unusual sites
 - Biopsy antrum for G-cell number (to distinguish between G-cell hyperplasia [↑G-cell number] vs G-cell hyperfunction (normal G-cell number); H. pylori
 - Thick gastric folds
- EUS for possible tumor localization
- Diagnostic imaging
 - Abdominal ultrasound
 - CT, head (pituitary fossa)
 - Octreotide scan
 - MBIG scan
 - CT scan of abdomen
 - MRI of abdomen
 - Parathyroid scan

Abbreviations: EUS, endoscopic ultrasound; ZES, Zollinger-Ellison syndrome

- The characteristics and clinical syndromes of functional Gut Endocrine Tumours

Type of tumour	Localization	% Frequency	Malignancy
➤ Carcinoid syndrome	Ileum, pancreas	90	100
➤ Insulinoma	Pancreas	10	
➤ Gastrinoma	Pancreas		5
➤ VIPoma	Pancreas	60	50-80
	Duodenum	25	

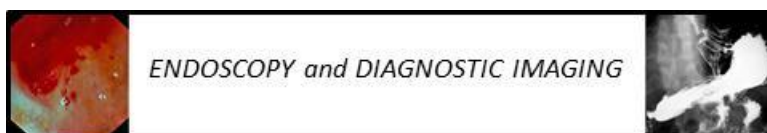


➤ Glucagonoma	Pancreas	90	90
➤ Somatostatinoma	Pancreas	56	90
	Duodenum	44	

*VIP – vasoactive intestinal peptide

➤ Clinical Syndromes

Name of syndrome	Signs/Symptoms	Hormone or peptide marker
➤ Gastrinoma (Zollinger-Ellison)	- Abdominal pain - Dyspepsia, diarrhea, MEN-1	Gastrin
➤ VIPoma/Verner Morrison	- Severe, watery diarrhea - Hypokalemia, dehydration	Diarrhea VIP
➤ Insulinoma	- Hypoglycemic symptoms	Insulin
➤ Glucagonoma	- Rash, anemia, weight loss, diabetes - Glucose intolerance - Thromboembolic disease	Glucagon
➤ Somatostatinoma	- Diabetes mellitus - Cholelithiasis - Diarrhea, steatorrhea	Somatostatin
➤ GRFoma	- Acromegaly	GRF
➤ Ppoma	- Weight loss, abdominal mass	PP
➤ CCKoma	- Often asymptomatic - Hypersecretion of pancreatic enzymes - Incomplete filling of fasting gallbladder	CCK
➤ Neurotensinoma	- Flushing, diarrhea	Neurotensin
➤ Ulcerogenic Tumour acid Syndrome with Non-gastrin secretagogue	- Abdominal pain - Dyspepsia - Diarrhea	Non-gastrin

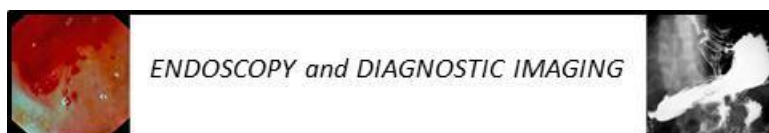


Mechanisms of Malabsorption in Zollinger-Ellison Syndrome

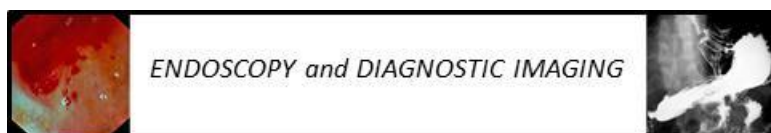
- Acidification and dilution of small intestinal contents → disturbances in physical-chemical events of fat digestion
 - Irreversible inactivation of pancreatic lipase, impaired formation of micellar lipid
 - Precipitation of bile salts (dihydroxyglycine conjugates); contributory factor by decreased formation of micellar lipid; unabsorbed bile acids may inhibit water and electrolyte transport in colon → diarrhea
 - Acid milieu inhibits transfer of fatty acid from oil to micellar phase
 - Excess fluid load presented to colon → diarrhea
 - Importance of gastric acid in items 1-3 underscored by the fact that diarrhea and steatorrhea are often ameliorated by measures directed at reducing acid output, i.e. Gastric aspiration, vagolytic drugs, PPI and total gastrectomy
- Structural changes in duodenal and jejunal mucosa
 - Changes are highly variable with patchy lesions including: blunted mucosa with absent villi; acute inflammatory exudate in lamina propria; edema, hemorrhage, microerosions; prominent Brunner's glands; abnormal surface epithelium
- Primary Biochemical Screening Program for MEN-1
 - Glucose
 - Albumin corrected total s-calcium
 - Parathyroid hormone
 - Prolactin
 - Insulin-like growth factor 1
 - Insulin
 - Proinsulin
 - Glucagon
 - Pancreatic polypeptide(PP)
 - Gastrin
 - Meal test with PP and gastrin analysis

Diagnostic imaging

- Narrowing
 - Benign
 - Peptic scarring
 - Granulomatous disease
 - Crohn's disease
 - Sarcoidosis
 - Tuberculosis
 - Syphilis

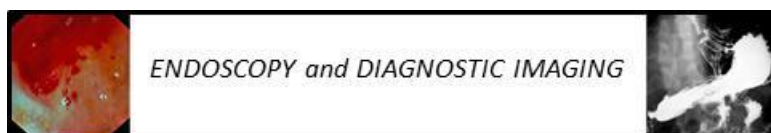


- Eosiphilic gastroenteritis
 - Corrosive ingestion
- Malignant
 - Scirrhou carcinoma
 - Adenocarcinoma
 - Lymphoma
 - Metastases
- Crohn's disease and other Granulomatosis disease
 - Narrowing – smooth, symmetrical, tapered, or uneven fibrosis, irregular deformity
 - Distal 1/3 of stomach, proximal duodenum (Crohn)
 - Tubular configuration (may be mistaken for Billroth I surgery; AKA “Ram's horn deformity”)
 - Non distensible
- Eosinophilic gastroenteritis
 - Nodular tapering of distal 1/3 of stomach
 - thick folds narrowing of distal stomach
- Caustic stricture
 - Degree of burn
 - 1st mucosa
 - 2nd submucosa, muscle layers
 - 3rd transmural
 - Stomach, duodenum
 - Large hematomas – intraluminal filling defects
 - Contraction of stomach
 - Atony
 - Rigidity
 - Irregular contour
 - Antral narrowing
- “Linitis plastica”
 - Scirrhou gastric adenocarcinoma
 - Metastases to stomach
 - Breast
 - Colon
- Piptic scarring
 - Antrum
 - Loss of antral shoulders
 - Duodenal changes



GASTRITIS

- The causes of histologically diagnosed gastritis
 - Drugs, chemicals, radiation
 - Medications
 - Aspirin, NSAIDs, COXIBs
 - Bisphosphonates, K+ tabs
 - Drugs, chemicals
 - Alcohol, bile, cocaine, chemotherapy, radiotherapy
 - Infection
 - Bacterial - H. pylori, Mycobacteria
 - Viral-CMV, HSV
 - Fungal
 - Parasitic
 - Graft-versus-host disease (GVHD)
 - Autoimmune gastritis (pernicious anemia)
 - Ischemia
 - Atherosclerosis
 - Sepsis
 - Burns
 - Shock
 - Mechanical ventilation
 - Associated with liver disease – GAVE, PHG
 - Trauma/foreign body
 - Nasogastric or gastrostomy tubes
 - Bezoar
 - Prolapse / sliding hiatal hernia/paraesophageal hernia
 - Cameron ulcer (ulcer in hiatus hernia)
 - Infiltration/ tumor
 - Lymphocytic/ collagenous
 - Granulomatous
 - Eosinophilic
 - Tumor
 - Miscellaneous
 - Gastritis cystica profunda
 - Ménétrier's disease (hyperplastic, hypersecretory gastropathy)



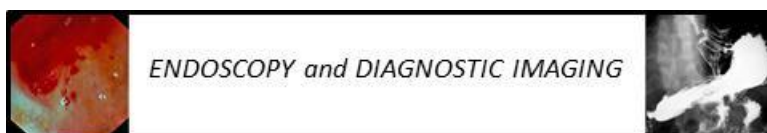
- The types of gastritis

Type of Gastritis	Etiologic Factors	Gastritis Symptoms
➤ Non-atrophic	○ Helicobacter pylori	- Superficial - Diffuse antral gastritis (DAG) - Chronic antral gastritis (CAG) - Interstitial – follicular - Hypersecretory - Type B
➤ Atrophic Autoimmune	○ Autoimmunity	- Type A - Diffuse corporal - Pernicious anemia associated
➤ Multifocal atrophic	○ Helicobacter pylori ○ Dietary ○ Environmental factors	- Type B - Environmental - Metaplastic

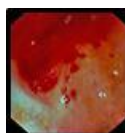
Useful background: Gastritis

➤ Special Forms

- Chemical
 - Chemical irritation (reactive)
 - Bile (reflux)
 - NSAIDs
 - Other agents (type C)
- Radiation
 - Radiation injury
- Lymphocytic (endoscopic)
 - Idiopathic (varioliform)
 - Immune mechanisms
 - Gluten (Celiac disease-associated)
 - Drugs (ticlopidine)
 - H pylori
- Non-infectious
 - Crohn's disease
 - Sarcoidosis
 - Wegener granulomatosis and other vasculitides
 - Foreign substances
 - Idiopathic (isolated granulomatous)



- Eosinophilic
 - Food sensitivity (allergic)
- Other infectious
 - Bacteria (no *H. pylori*)
 - Phlegmonous
- Gastrides
 - Viruses
 - Fungi
 - Parasites
- Gastric Inflammatory Conditions: Nosologic Entities
 - Infectious gastritis (*H. Pylori*, TBC, CMV, parasites, bacterial overgrowth)
 - Auto-immune gastritis
 - Drug-associated gastritis (aspirin, NSAID, alcohol)
 - Rugal hyperplastic gastritides (Ménétrier; hypersecretory)
 - Granulomatous gastritides (Crohn, idiopathic)
 - Enterogastric reflux gastritis
 - Physical /chemical caustic gastritides (radiation, lye)
 - Stress-associated gastritis
 - Vascular gastritides (ischemia, vasculitis)
 - Miscellaneous (idiopathic erosive, eosinophylic, pseudolymphomatous, collagenous, etc.)
- Phlegmonous Gastritis
 - acute bacterial inflammation of mucosa and submucosa (usually hemolytic streptococci; usually prior debility, rarely prior ischemic necrosis)
 - severe erythema/exudate or erosive gastritis
 - severe acute gastritis
 - severe abdominal pain simulating an acute abdomen
 - purulent vomiting
 - broad spectrum antibiotics
- Enterogastric reflux gastritis
 - Reflux of biliary and pancreatic juice
 - Conversion of lecithin into lysolecithin through pancreatic and possibly *H.pylori* phospholipase A2
 - Increased lysolecithin lowers mucus layer hydrophobicity
 - Lowering of hydrophobicity reduce's mucosal defence against acid



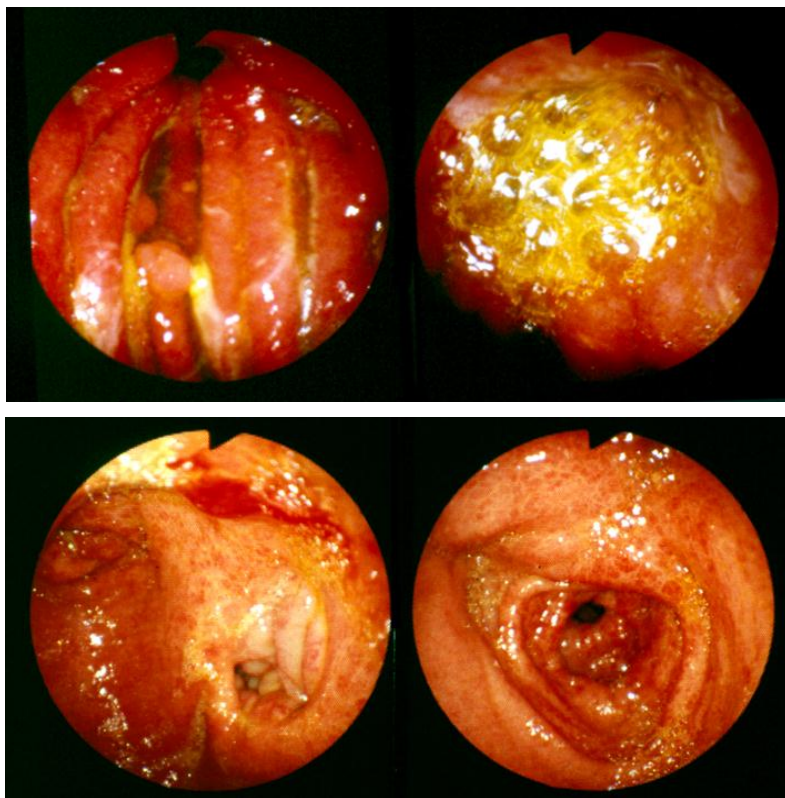
ENDOSCOPY and DIAGNOSTIC IMAGING

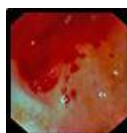
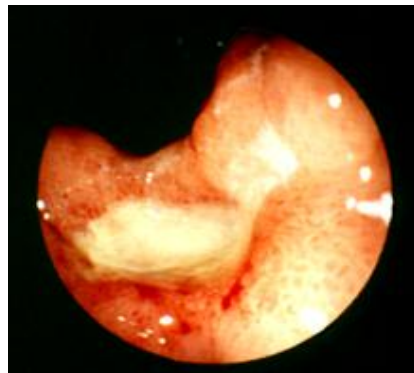
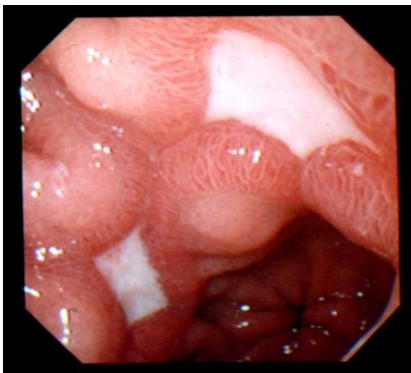
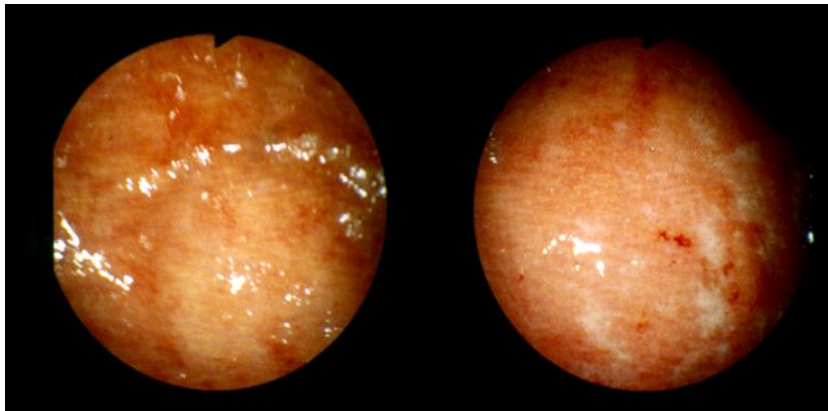
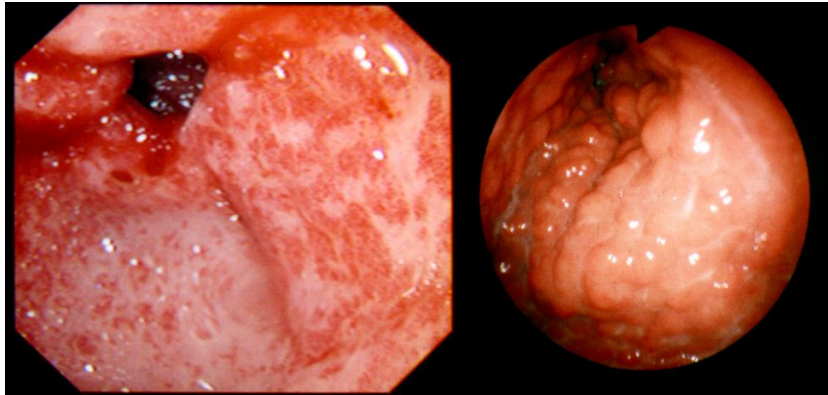


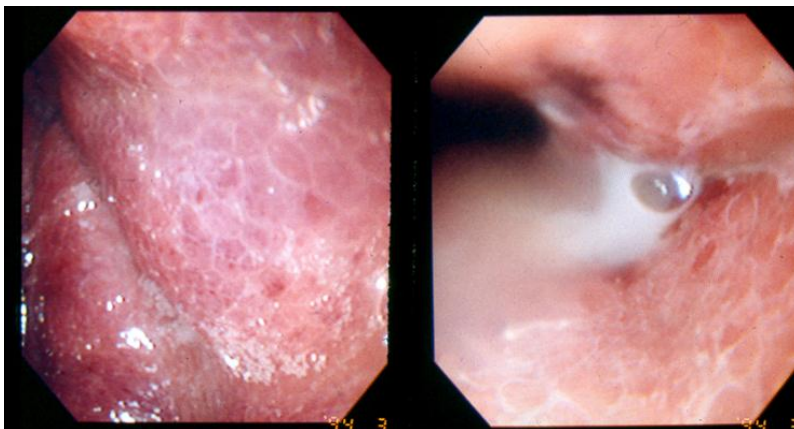
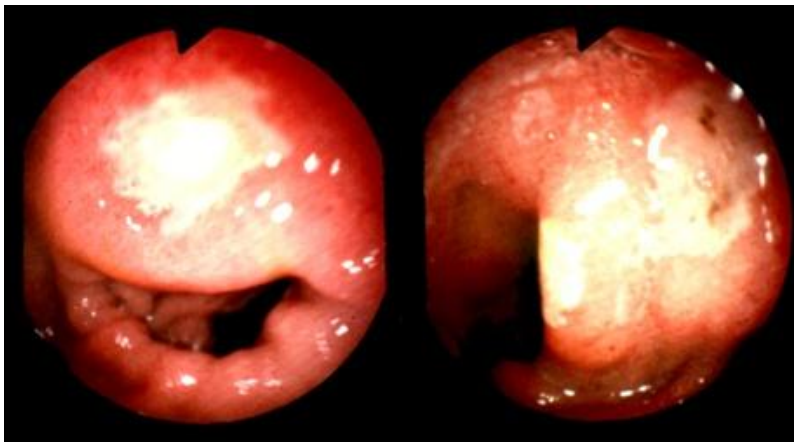
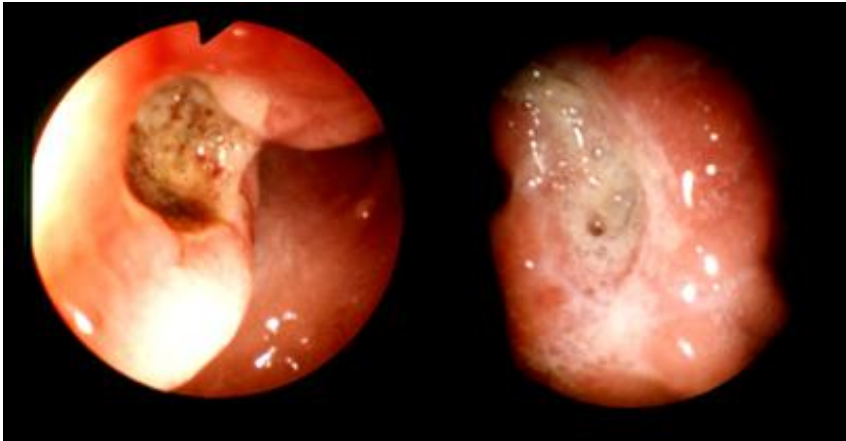
At EGD, why biopsy when the mucosa appears to be endoscopically normal?

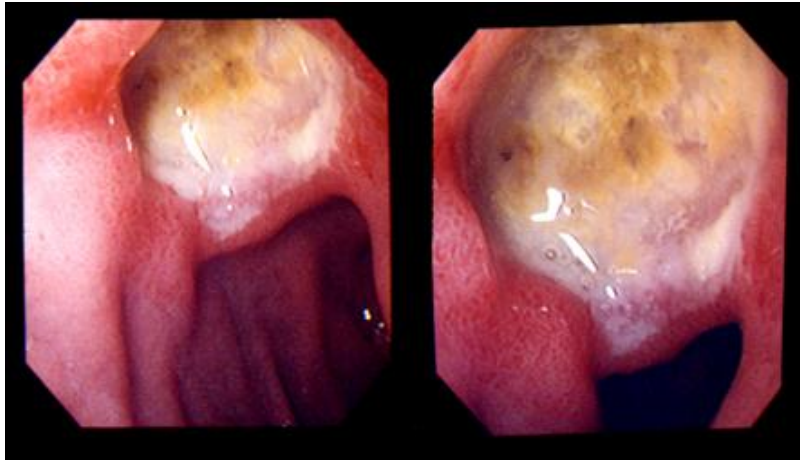
- To contribute in unravelling the cause of symptoms, justifying the endoscopy
- To detect and grade histologic gastritis
- To detect uncommon causes of gastritis (eg. infections, granulomatous, eosinophilic, vasculitis)
- To detect atrophy and intestinal metaplasia
- To detect (early) dysplasia

➤ Enterogastric reflux – associated gastritis





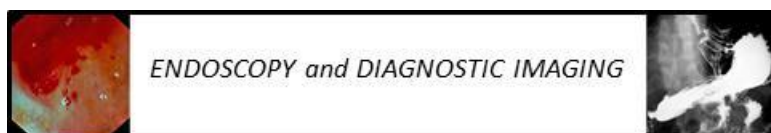




Eosinophilic gastritis

- The disorders with moderate eosinophilia 1,000 to 5,000/mm³
 - Allergic Disorders
 - Asthma
 - Urticaria
 - Eczema
 - Drug Allergy
 - Parasitic infections
 - Ascariasis
 - Schistosomiasis
 - Anisakiasis (*Eustoma rotundatum*)
 - Trichinosis
 - Tropical eosinophilia – probably due to microfilaria
 - Echinococcosis
 - Liver Fluke
 - Collagen-vascular diseases
 - Rheumatoid arthritis
 - Polyarteritis nodosa
 - Gastrointestinal Diseases
 - Eosinophilic gastroenteritis
 - Ulcerative colitis
 - Crohn's disease
 - Neoplasia
 - Chronic myelogenous leukemia
 - Hodgkin disease
 - Other lymphomas
 - Carcinoma (lung cancer)
 - Radiation-related eosinophilia

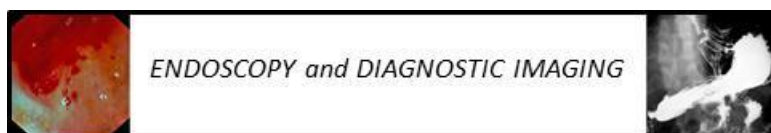
- Miscellaneous
 - Pulmonary infiltrates with eosinophilia
 - Chronic peritoneal dialysis
 - Hereditary eosinophilia
- Disorders with marked eosinophilia
 - Parasite infestations:
 - Visceral larva migrans associated with toxocara canis or cati infestation
 - Tissue migration during larval stage, including ascaris, trichinella, hookworm strongyloides, fasciola hepatica
 - Disseminated eosinophilic collagen disease or hypereosinophilic syndrome
 - Eosinophilic leukemia
 - Hodgkin disease
 - Miscellaneous disorders, including drug sensitivity and polyarteritis nodosa
- The clinical features, pathology, radiological features, differential diagnosis and complications of eosinophilic disorders of the GI tract
- Clinical features
 - Recurrent episodic gastrointestinal symptoms
 - cramping abdominal pain
 - nausea and vomiting
 - diarrhea
 - weight loss
 - Hypoproteinemia; edema
 - Malabsorption - steatorrhea; hypocalcemia
 - Symptoms related to anemia - fatiguability; dyspnea
 - Eosinophilic ascites or pleural effusion
- Pathology
 - Predominant mucosal disease
 - Fecal blood loss
 - Iron deficiency anemia
 - Intestinal protein loss with hypoproteinemia
 - Diarrhea
 - Fat malabsorption
 - Predominant muscle layer disease
 - Pyloric narrowing and stomach outlet obstruction
 - Segmental small bowel involvement
 - Predominant subserosal disease
 - Eosinophilic ascites
- Complication



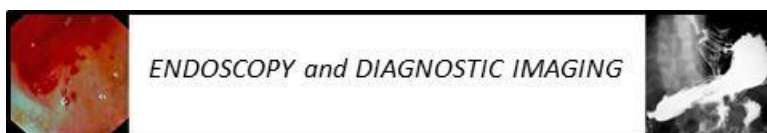
- Intestinal complications
 - Protein loss
 - Fat malabsorption
 - Iron deficiency
 - Vitamin B12 deficiency
 - Gastric outlet obstruction
 - Small bowel obstruction
 - Bacterial overgrowth
 - Gastrointestinal hemorrhage
- Extra-intestinal complications
 - Mesenteric adenitis
 - Hepatosplenomegaly
 - Bone marrow eosinophilia
 - Eosinophilic pleuritis and peritonitis
 - Eosinophilic pancreatitis
 - Eosinophilic cystitis
 - Systemic reactions to food
- Differential diagnosis
 - Allergic gastroenteropathy
 - Crohn's disease
 - Carcinoma or lymphoma
 - Parasitic infestation
 - Tropical sprue, celiac sprue, Whipple disease
 - Periarteritis nodosa
 - Amyloidosis
 - Tuberculosis
 - Allergic granulomatosis
 - Disseminated eosinophilic collagen disease

Useful background

- Allergic gastroenteropathy
 - Mainly in first and second decades
 - Growth retardation, edema
 - ↓ Albumin, ↓ globulin, protein losing
 - Anemia, blood eosinophilia
 - Manifestations of allergy (asthma, eczema, allergic rhinitis)
 - Small bowel eosinophilic infiltration in mucosa and submucosa
 - Definite history of allergy to milk proteins or meat
 - Favourable response to elimination diet or corticosteroids
- Disseminated eosinophilic collagen disease
 - Middle age, mainly male patients
 - Persistent eosinophilia in blood

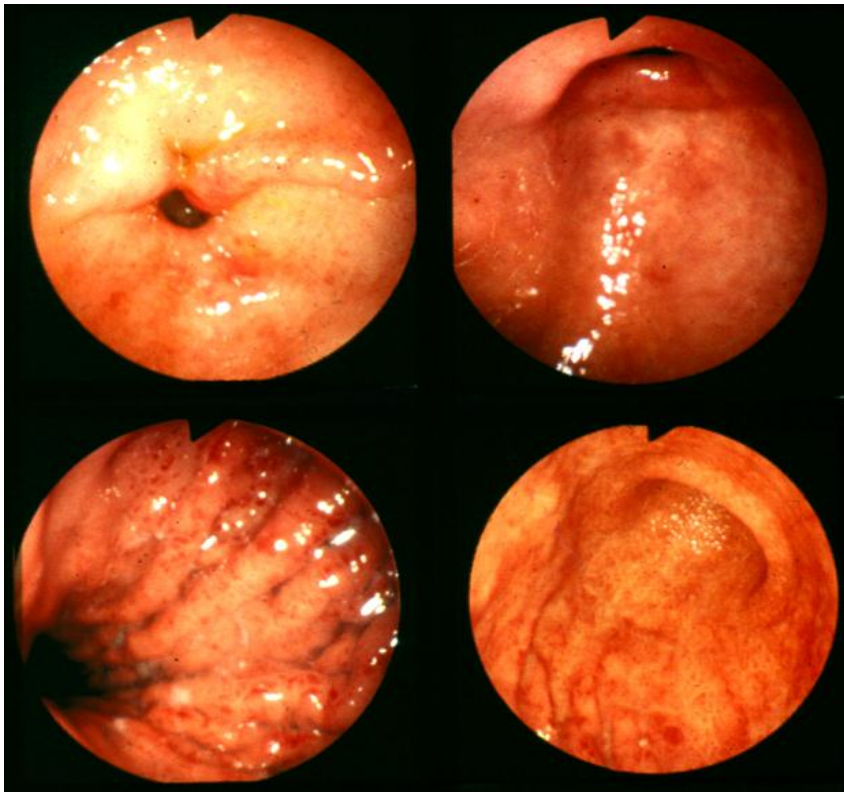


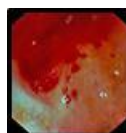
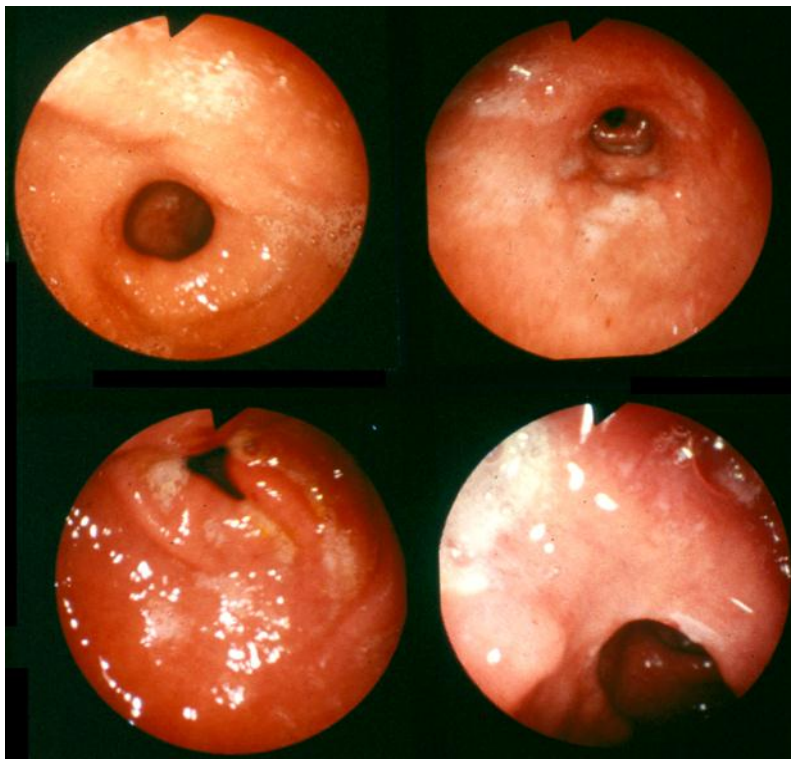
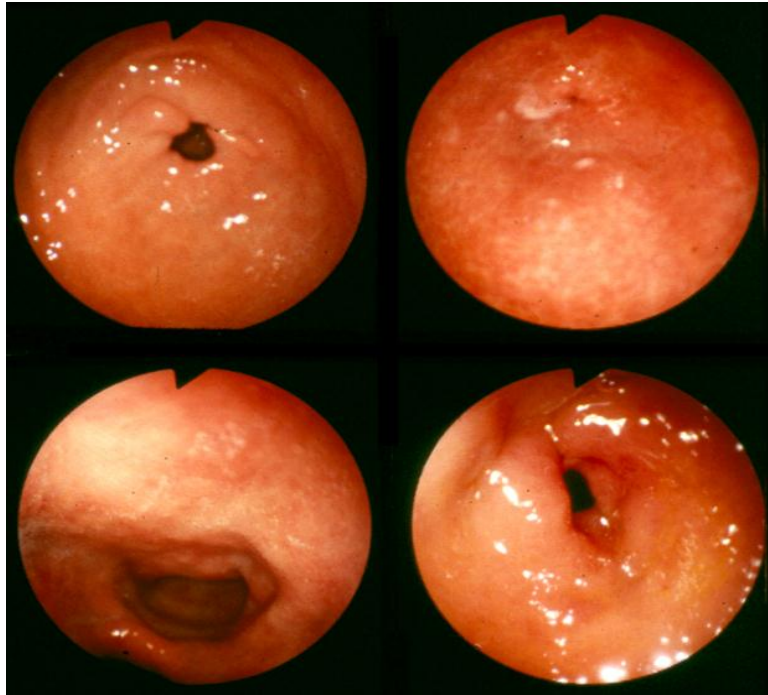
- Diffuse organ infiltration by eosinophils (hepatosplenomegaly, heart disease, nervous system abnormalities, pulmonary disease)
 - No other cause for eosinophilia (infectious or parasitic disease, neoplasia, etc)
 - Fever, anorexia, and weight loss, recurrent abdominal pain, persistent non-productive cough with chest pain, various neurologic abnormalities, pruritic rash, congestive heart failure, hepatosplenomegaly, lymph-adenopathy
 - Significant morbidity and mortality (average survival)
- The hypereosinophilic Syndrome (HES): Loeffler Fibroplastic Endocarditis
- Middle age, mainly male patients
 - Persistent hyper-eosinophilia in blood >1500 eos/mm³
 - diffuse organ infiltration by eosinophils (hepatosplenomegaly, heart disease, nervous system abnormalities, pulmonary disease, fever, weight loss, anemia)
 - No other cause for eosinophilia (infectious or parasitic disease, neoplasia, etc)
 - Fever, anorexia, and weight loss, recurrent abdominal pain, persistent non-productive cough with chest pain, various neurologic abnormalities, pruritic rash, congestive heart failure, hepatosplenomegaly, lymph-adenopathy
 - Significant morbidity and mortality (average survival 9 months) despite corticosteroids and/or antileukemic drugs
 - Cardiovascular pulmonary, hematopoietic, and nervous system most often involved, hepatic, dermatologic, gastrointestinal and renal involvement less frequent
- Radiological
- Enlarged gastric rugal folds - antral narrowing and rigidity - irregular intraluminal mass
 - Thickening and widening of valvulae conniventes
 - Regular nodular contour defects
 - Distorted valvulae with irregular angulation and saw-toothed contour
 - Luminal narrowing with rigid effaced folds
 - Separation of intestinal loops
 - 'Dysfunction pattern'
 - Polypoid colonic defects
- Gastric inflammatory conditions: nosologic entities
- Infectious gastritis (*H. Pylori*, TBC, CMV, parasites, bacterial overgrowth)
 - Auto-immune gastritis
 - Drug-associated gastritis (aspirin, NSAID, alcohol)

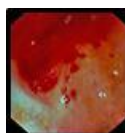
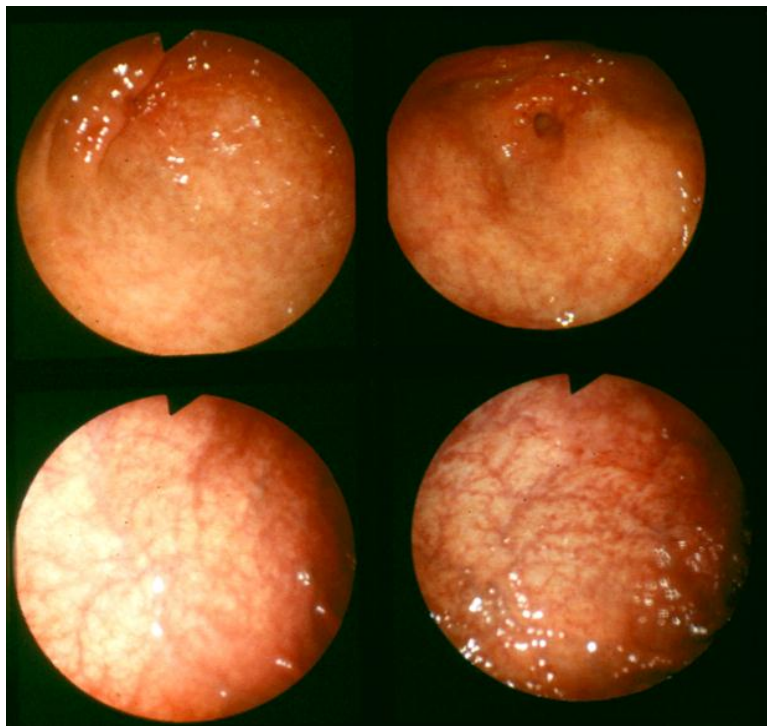
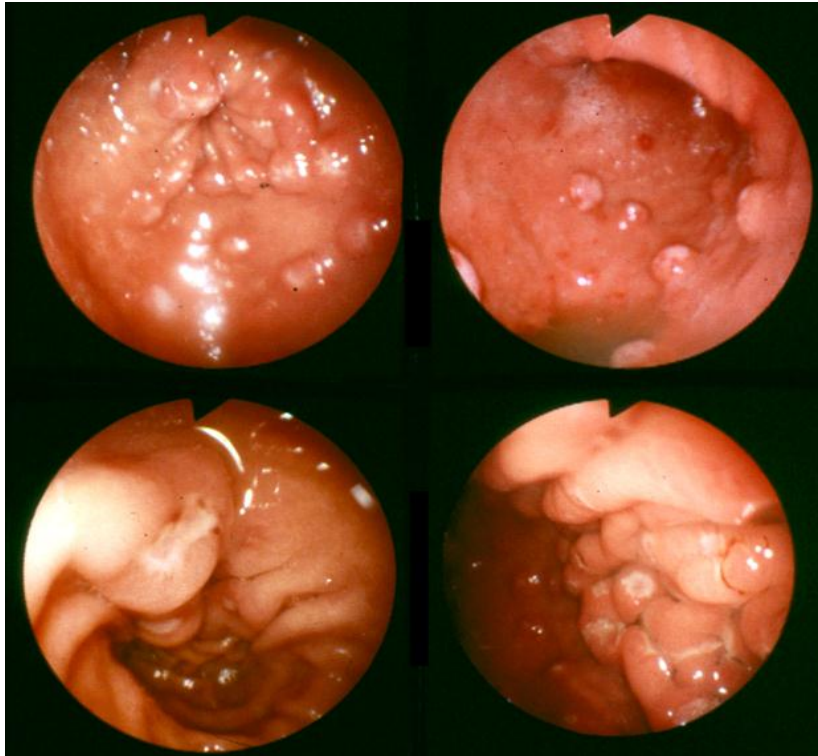


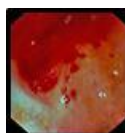
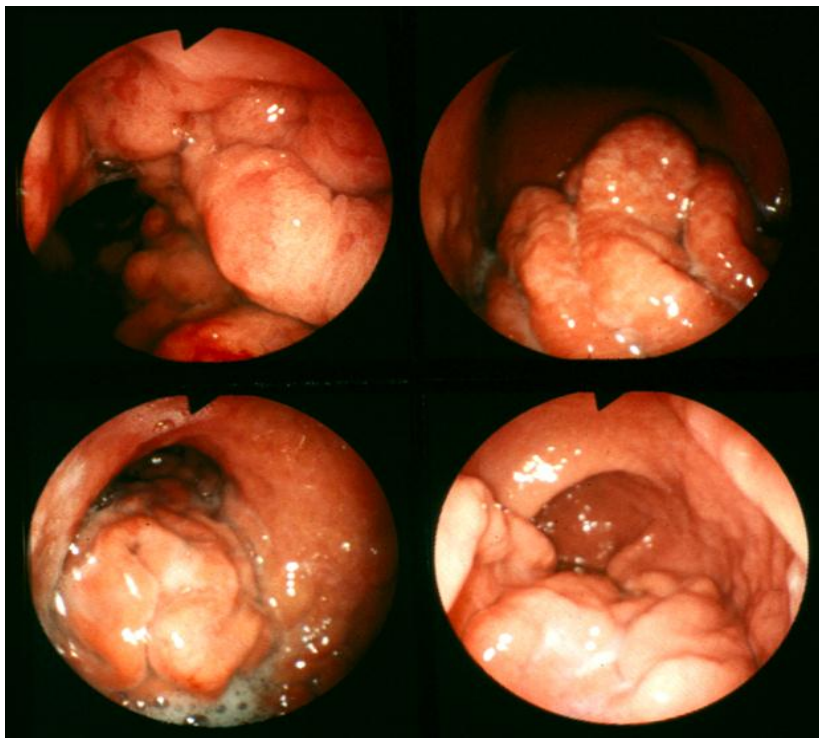
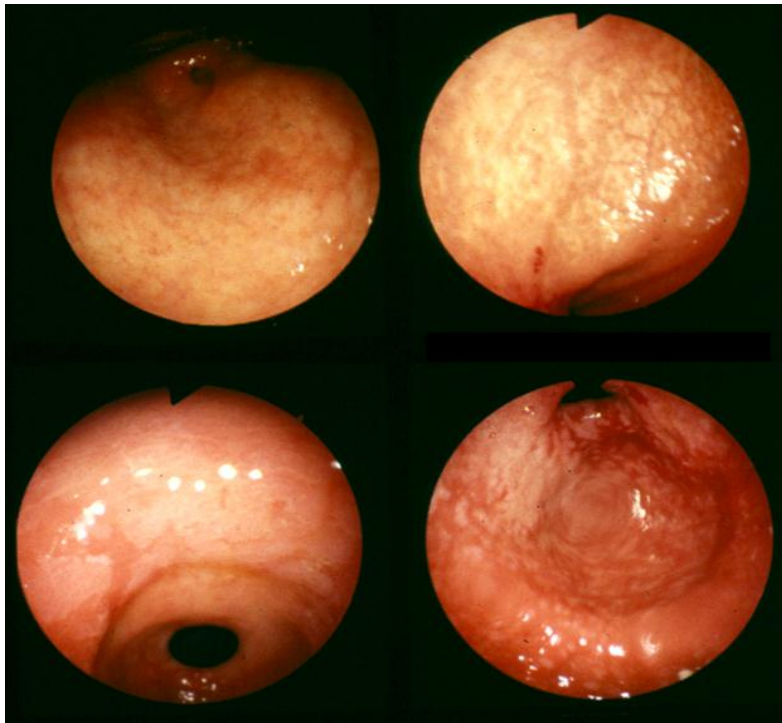
- Rugal hyperplastic gastritis (Ménétrier; hypersecretory)
- Granulomatous gastritis (Crohn, idiopathic)
- Enterogastric reflux gastritis
- Physical /chemical caustic gastritis (radiation, lye)
- Stress-associated gastritis
- Vascular gastritis (ischemia, vasculitis)
- Miscellaneous (idiopathic erosive, eosinophylic, pseudolymphomatous, collagenous, etc.)

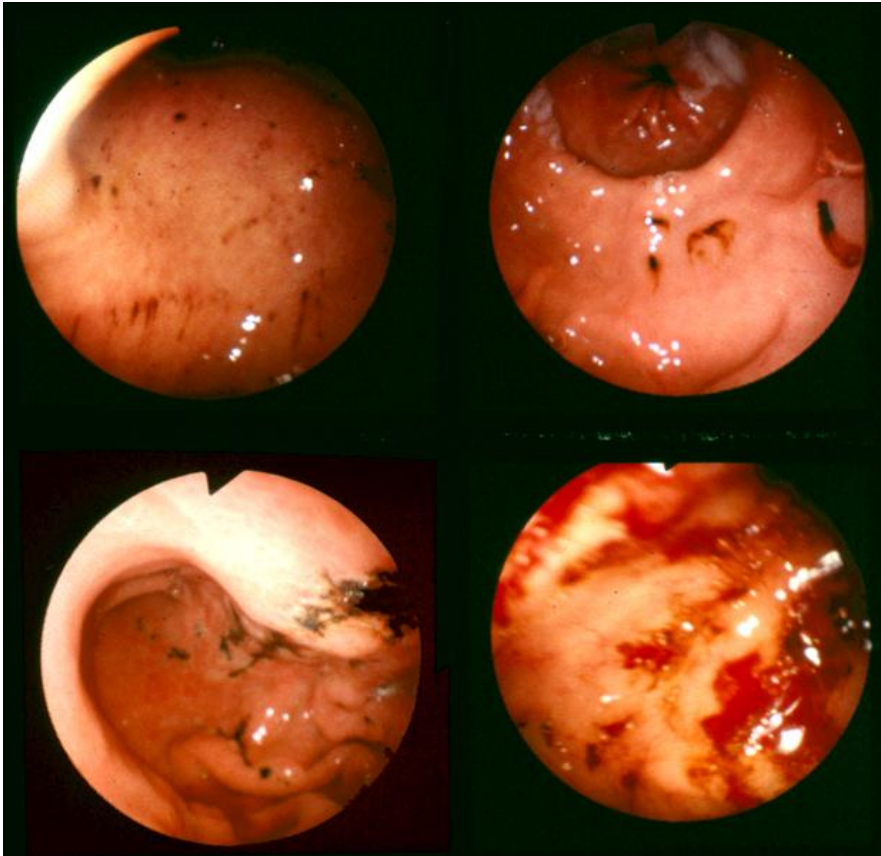
Diagnostic imaging of gastritis











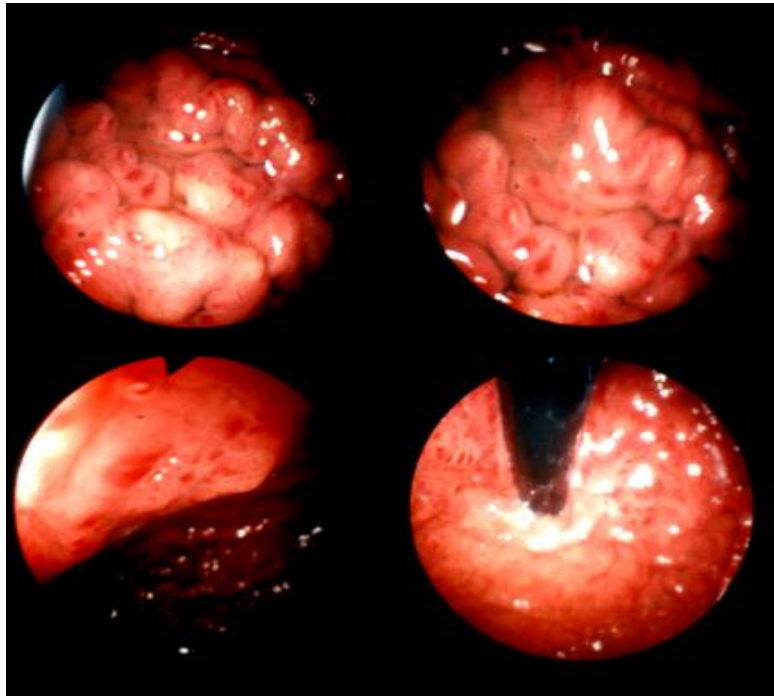
➤ Phlegmonous gastritis

- Pg acute bacterial inflammation of mucosa and submucosa (usually hemolytic streptococci; usually prior debility, rarely prior ischemic necrosis)
- En severe erythema / exudate or erosive gastritis
- Hi severe acute gastritis
- Sy severe abdominal pain simulating an acute abdomen; purulent vomiting
- Tx broad spectrum antibiotics

➤ Congestive gastropathy: endoscopic appearances

- Mild – Scarlatina (fine pink speckling)
- Moderate – More pronounced pathy reddening – striped appearance
 - Snake skin (quite specific) – white reticulated pattern
- Severe – Cherry red spots – diffuse hemorrhagic

➤ Portal hypertensive gastropathy

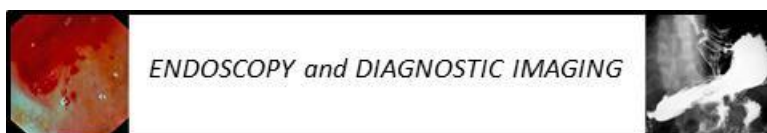


PEPTIC ULCER DISEASE (PUD)

Dyspepsia

- The benefits and limitations associated with 5 interventional/ diagnostic approaches to the patient with dyspepsia who is under 50 years of age and who has no alarm symptoms.

Diagnostic approach	Benefits	Limitations
○ “Watchful waiting” only	- Patients with mild and transient symptoms are not prescribed medication or investigated	No clinical studies.
○ Empirical Antisecretory therapy (PPI or H2RA)	- Addresses symptoms immediately - Documented effect on reflux symptoms and ulcer-related symptoms	Recurrence after therapy is the rule. EGD is often only postponed, and may be false negative.
○ Treat based on clinical diagnosis	- Clinically meaningful. Low costs	Unreliable.
○ Treat based on subgrouping and computer-based algorithms	- Clinically attractive. Low costs	Does not reliably predict EGD diagnosis or response to therapy
○ <i>H.pylori</i> test-and-treat	- Infected patients with ulcer disease will have symptomatic benefits. Reduces endoscopy rates. Safe and cost-effective compared with endoscopy. Possible reduced risk of later ulcer development.	Low benefit in those without peptic ulcer disease will not benefit. Continuing or recurrent symptoms may frustrate patients and clinician
○ <i>H.pylori</i> test-and-scope	- Potential to reduce upper EGD rates in <i>H. pylori</i> low-prevalence areas	Only meaningful if a decision about eradication therapy in infected patients is influenced by endoscopy result. Increases endoscopy demands. Not applicable in <i>H. pylori</i> -high prevalence areas
○ Early endoscopy	- Diagnostic “gold standard”. Might lead to reduced medication in patients with normal findings. Increased	Invasive. Costly. About half of EGDs will be normal. Long waiting lists may lead to false negative results. Not the preferred option for many



patient satisfaction in some trials.

patients. Does not diagnose non-erosive reflux disease (NERD).

Abbreviations: EGD, esophagogastroduodenoscopy; H2RA, H2 receptor antagonist; NERD, non-erosive reflux disease; PPI, proton pump inhibitor.

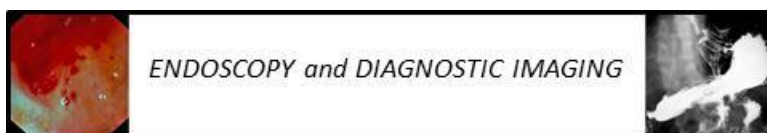
Adapted from: Bytzer P. *Best Practice & Research Clinical Gastroenterology* 2004;18(4): p.683.

- Management strategies in the person with dyspepsia
 - Empiric Treatment
 - Treat with antisecretory, promotility or antibacterial drugs.
 - Investigation reserved for treatment failures
 - Test and treat
 - Testing for *H. pylori* by serology ? Urea breath test.
 - Treat all positive cases with anti-bacterial therapy
 - Test and investigate
 - Testing for *H. pylori* and reserving endoscopy for positive cases
 - Investigate
 - Immediate diagnostic evaluation by endoscopy.
 - Target therapy based on results

In persons with an *H. Pylori* infection plus dyspepsia, *H. Pylori* eradication decreases the mean dyspepsia score but has no effect on the person's quality of life (Bektas et al. 2009).

Recent Updates: When to Perform EGD in Dyspepsia

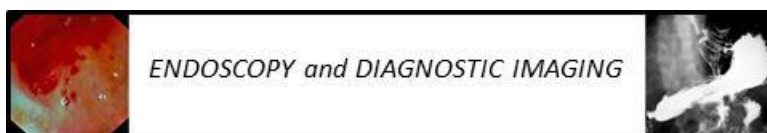
- There is a poor correlation between dyspeptic symptoms and findings at EGD (Zagari et al., 2010; Thomson et al., APT 2003; 17: 1481-91; Vakil, AJG 2010; 105: 512-4). Attempts to predict the pre-EGD probability of finding a serious lesion have included the patient's age, the presence of "red flags", a family history of esophageal/ gastric cancer, or belonging to a demographic group with such as high risk (eg. in Canada, persons with a high risk of an *H. Pylori* infection, "new Canadian" from a high endemic area).
- Barrett's persons with a high pre-test probability of Barrett's epithelium include middle-aged Caucasian males, or a person with a long (>5 year) history of moderate/severe heartburn occurring more than 3 times per week). Even the presence of alarm symptoms/signs such as vomiting, anemia/bleeding, dysphasia or weight loss have a relatively low sensitivity and specificity to identify the persons with a high probability of having dysplasia or



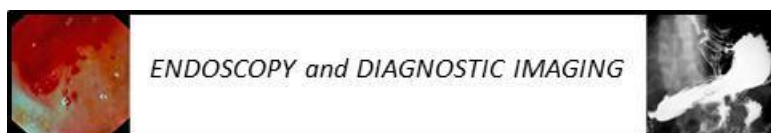
cancer, and therefore requiring an EGD in the management of their symptoms. About two-thirds of persons with alarm symptoms/signs have a normal EGD, and less than 10% of dyspeptic persons with alarm symptoms will have a neoplasia (Zoggari et al., AJG 2010; 105; 105; 565-71).

Useful background: Dyspepsia and pregnancy

- Upper GI symptoms are common in pregnant women, and when EGD has been performed the findings are esophagitis (34%) and gastritis (25%).
 - Predictors of heartburn during pregnancy include young age of the mother, her parity, increasing gestational age, and the presence of heartburn before pregnancy (which occurs in 14% of mothers) (Marrero JM, et al. *Br J Obstet Gynaecol* 1992:731-4).
 - Only calcium-containing antacids should be used for GERD symptoms, since aluminum-containing antacids may cause fetal neurotoxicity, alginic acid (Gaviscon) may cause fetal distress, and magnesium-containing antacids may cause a number of fetal disorders (renal stones, respiratory distress and cardiovascular impairment, and hypoxemia, especially when used in higher doses for longer intervals) (Katz 09).
 - Nizatidine is not recommended for lactating mothers (FDA C, due to report of growth retardation of rodent pups)
- The long-term consequences of Acid Inhibition with PPIs
 - Peculiarities of Intragastric Acidity
 - Effects on gastric pH
 - Nocturnal acid breakthrough
 - Tachyphylaxis?
 - Rebound?
 - Nocturnal Acid Breakthrough (pH<4 for >1 hr)
 - Occurs in up to 70% of GERD patients treated with PPI bid, especially Hp-negative
 - Acid rebound
 - Occurs 7 days following cessation of 2-3 months high-dose PPI treatment
 - Increases BAO but more consistently MAO (but an unphysiological stimulus)
 - May last up to 11 months
 - May not be seen in *H. pylori*-positive patients



- Mechanism uncertain? Hypergastrinemia ® enterchromaffin cell hyperplasia
- Relevance to symptom relapse?
- Increased Risk of Enteral Infection
 - One case of bacterial diarrhea per 3,319 PPI prescriptions!
 - PPI therapy may be a risk factor for campylobacter enteritis (Odds ratio 11.7)
- Bacterial Overgrowth (small intestinal)
 - Most obvious in Hp-positive persons
 - High nitrite levels
 - Low ascorbic acid levels → more N-nitroso compounds
- Altered Metabolism of Alcohol
 - Bacterial overgrowth particularly aerobes causes acetaldehyde production from alcohol-acetaldehyde is a local carcinogen
 - Poor acetaldehyde metabolizers due to mutant ALDH2 have 2-3 times higher in vivo salivary acetaldehyde levels after moderate amounts of alcohol (oriental flushers)
- The adverse Factors for DU, (duodenal ulcer) Healing and Recurrence
- Clinical
 - Smoking
 - Severe, prolonged pain on last relapse
 - Pain radiating into the back
 - Male
 - Positive family history
 - Onset when young
 - Symptoms slow to respond
 - Vomiting
 - Previous complication
- Endoscopic
 - Linear ulcer
 - Multiple ulcers
 - ulcer on linear scar
 - Deep crater
 - Narrow lumen
 - Persistent duodenitis after healing



Helicobacter pylori infection (H.pylori)

Useful background: H. Pylori

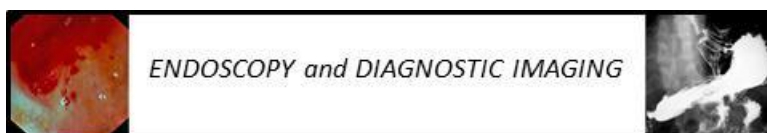
- DU occurs in duodeno/antral transitional zone or in areas of gastric metaplasia
 - Chronic acid peptic jet from the stomach contributes to focal mucosal injury and metaplasia?
 - Less mucosal bicarbonate secretion in vulnerable areas?
 - *H. pylori* infection of transitional zone or metaplastic areas leads to inflammation, epithelial destruction, coalescing erosions and ulceration (microinfarction)
 - GU occurs in antral type mucosa bordering corpus-type mucosa
 - Speculated
 - Mucosal boundaries are inherently unstable
 - More acid along lesser curve
 - Restricted mural blood flow
 - Higher *H. pylori* density, more pronounced alteration of mucus layer, more extensive mucosal damage
 - More mural stretching
 - The urease activity of *H. Pylori* provide a means for the organism to burrow through the mucus overlying the gastric epithelium to bind to adhesions, and to caloricize the alkaline environment adjacent to the membrane. It invades the gastric mucosa, while being able to evade the host immunity. The adhesions provide an interplay between bacterial and List Lewis antigens, and help to determine different clinic-pathologic outcomes (Sheu et al. 2010). IL-1 and TNF- α gene clusters are important in defining the extent and severity of *H. Pylori* associated gastritis. The common pan-gastritis may or may not be symptomatic, the antral predominant gastritis is associated with an increased risk of duodenal ulcer disease, and gastric body associated gastritis is associated with multifocal gastric atrophy and an increased risk of gastric cancer (Shanks and El-Omar 2009).
 - Modes of transmission of *H. pylori* (Hp), and the impact of one person in the family being positive for *H. pylori* on the rate of *H. pylori* infection by others in the family.
- Modes of transmission of Hp
- Gastro-oral vomitus-oral, fecal-oral
- The impact of an infected family member on others in the family group
 - Hp positive parent
 - spouse 68% Hp⁺



- children 40% Hp⁺
- Hp negative parent
 - spouse 9% Hp⁺
 - children 3%Hp⁺
- Community Risk
 - Adults - approximately 25-30% (depends on person's age)
 - Higher (30%) in older persons
 - >50% First Nations Canadians, new Canadians from high Hp prevalence areas
 - New Canadians from high prevalence countries

Practice Pointers:

- There is a broad range of tests available to diagnose the presence of an H. pylori infection
 - Put only upper endoscopy plus biopsy for histological examination or culture will provide a diagnosis of H. pylori, plus H. pylori
 - associated disease such as gastritis, peptic ulcer disease intestinal metaplasia, gastric cancer or mALT lymphoma (Guarner et al. 2010).
 - The culture of the gastric biopsies also provides for testing for in vitro antibiotic sensitivity of the organism, as well as gene testing for antibiotic resistance, but the sensitivity is low.
 - The rapid urease tests have better sensitivity than less histology.
 - The non-tissue, non-endoscopy tests include blood, breath and stool antigen testing. The urea breath test is more than 75% sensitive and can be used both to diagnosis an H. pylori infection and to confirm its eradication.
 - Testing for H. pylori antigens in stool is also useful before and after treatment, and has greater than 95% sensitivity.
- GI and non-GI conditions which may be associated with H. pylori (Hp) infection.
- Hp-associated GI Diseases
 - Acute/chronic gastritis
 - Duodenal and gastric ulcer (DU and GU) (only ~20% of Hp⁺ persons develop disease)
 - Accentuation of effect of smoking on PUD
 - Accentuation of ASA/NSAID effects on peptic ulcer disease (synergeneity)
 - Non-ulcer dyspepsia
 - Atrophic gastritis – intestinal metaplasia- dysplasia – GCa gastric (non-cardia)
 - Maltoma



- Fundic gland polyps
 - Hypertrophic gastric folds
 - Protective against GERD
 - Halitosis
 - Carcinoid tumors (hypochlorhydria)
 - Colorectal cancer (possible association, due to hypergastrinemia)
 - Pancreatic cancer (possible)
- Possible Hp-associated non-GI diseases
- Head –otitis media, migraines, headaches
 - CNS – Parkinsonism, CVA
 - Heart – atherosclerotic diseases
 - Lung – chronic bronchitis, COPD, SIDS
 - Blood – ITP, iron deficiency
 - Skin – idiopathic chronic urticaria, acne, rosacea
 - Growth retardation in children

Abbreviations: CVA, Cerebrovascular accident; COPD, chronic obstructive pulmonary disease; DU, duodenal ulcer; GCa, gastric cancer; GERD, gastroesophageal reflux disease; GU, gastric ulcer; ITP, idiopathic thrombocytopenic purpura; PUD, peptic ulcer disease; SIDS, sudden infant death syndrome.

Adapted from: Hunt R. *AGA Institute Post Graduate Course 2006*; pg. 333-342.; and Graham DY. and Sung JJY. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management 2006*. pg. 1054.

- Recommended indications for *H. pylori* eradication therapy (ET) in the patient taking NSAIDs or ASA.
 - Reduce PUD formation
 - Reduce recurrent PUD
 - Reduce recurrent PUD bleeding (in ASA or NSAID high risk users) (ET does not prevent further PUD bleeding in high risk ASA/NSAID users on PPI)

Abbreviation: ET, eradication therapy

Adapted from: Lai LH., and Sung JJY. *Best Practice & Research Clinical Gastroenterology 2007*; 21(2): pg. 270.

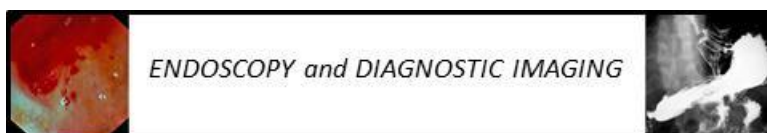
- The causes of Recurrent Peptic Ulcer After Eradication of *H. pylori* infection
 - *H. pylori* reappearance / almost always recrudescence not reinfection
 - Surreptitious intake of aspirin/NSAIDs



- Poor mucosal healing due to excessive scarring
- *H. pylori*-negative DU with abnormally high acid response
- Other conditions (e.g. gastrinoma, Crohn's disease)
- Idiopathic duodenal ulcer disease
- *H. pylori* virulence factors
 - Cag A translocated within epithelial cell by cag-encoded type IV secretion system (~ Tir of EPEC)
 - After injection, bacterial protein is recognized as a host-encoded protein, tyrosine-phosphorylated and activated
 - Activated Cag A triggers cortical actin reorganization by N-WASP and Arp 2/3 interactions and nuclear signals mediated by the Rho GTP-ases and the JNK pathway
- CagA pos, VacA s1 strains (ulcer patients)
 - More inflammation
 - Lower bacterial load
 - Better penetration of antibiotics
 - Easier to cure
- CagA neg, VacA s2 strains (FD patients)
 - Less inflammation
 - Higher bacterial load
 - More difficult to cure

Practice Pointers: *Helicobacter pylori* :Newer Treatment Regimens

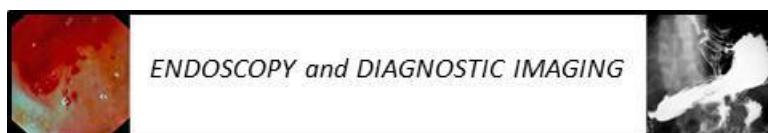
- Who should receive *H. pylori* Eradication therapy?
 - All NSAID users
 - High-risk patients
 - Patients starting NSAIDs
 - Patients stopping NSAIDs
 - Patients with a GU
 - Patients with a DU
 - Patients taking COX-2 inhibitors (Coxibs)
 - Patients taking aspirin (ASA)
 - Possibly patients taking antiplatelet agents
 - Possibly patients with dyspepsia while on NSAIDs/ ASA/ Coxibs
- Meta-analysis of *H. pylori* eradication therapy in FD
 - Anti-*H. pylori* treatment superior to placebo ($p=0.0002$)
 - Resolution of symptoms in 9% more anti-*H. pylori* treated versus placebo treated patients (95% CI = +4% to +14%)



- No evidence of heterogeneity or of bias publication of positive results
- Meta-analysis does not show a statistical difference in *H. pylori* eradication rates whether using triple or quadruple therapy (RR = 1.002; 95% CI 0.936-1.073) (Luther J Schoenfeld P, et al. *Am J Gastroenterol* 2008:S397.)
- Meta-analysis showed 93% eradication rate with sequential therapy versus 74% for clarithromycin-based triple therapy (Jafri N, et al. *Ann Intern Med* 2008:2220-2223), particularly in persons with clarithromycin-resistant strains of *H. pylori*. None of the *H. pylori* treatment guidelines endorse sequential therapy yet (Chey 09).
- Meta-analysis has shown superiority of a 10-day course of levofloxacin-based triple therapy and a 7 day course of bismuth-based quadruple therapy (rr = 0.51; 95% CI: 0.34-0.75) for persistent *H. pylori* infection (Saad R Schoenfeld P, et al. *Am J Gastroenterol* 2006:488-96.)
- Rifampin has been used as an alternative to clarithromycin, with EE of 38-91% (Chey WD, Wong BC. *Am J Gastroenterol* 2007:1808-1825) but there may be rare but serious adverse effects (myelotoxicity and ocular toxicity).
- Furazolidone used in place of clarithromycin, metronidazole or amoxicillin gives EE of 52-90% (Chey WD, Wong BC. *Am J Gastroenterol* 2007:1808-1825).

Practice Pointers:

- Diagnostic Tests of *H. pylori*
 - Invasive
 - Rapid urease test
 - Histology
 - Culture
 - PCR
 - Non-invasive
 - Antibody detection
 - Serum-ELISA (quantitative)
 - Immunoblot (qualitative)
 - ¹³C, ¹⁴C urea breath test



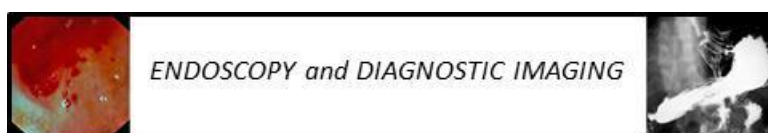
Practice Pointers:

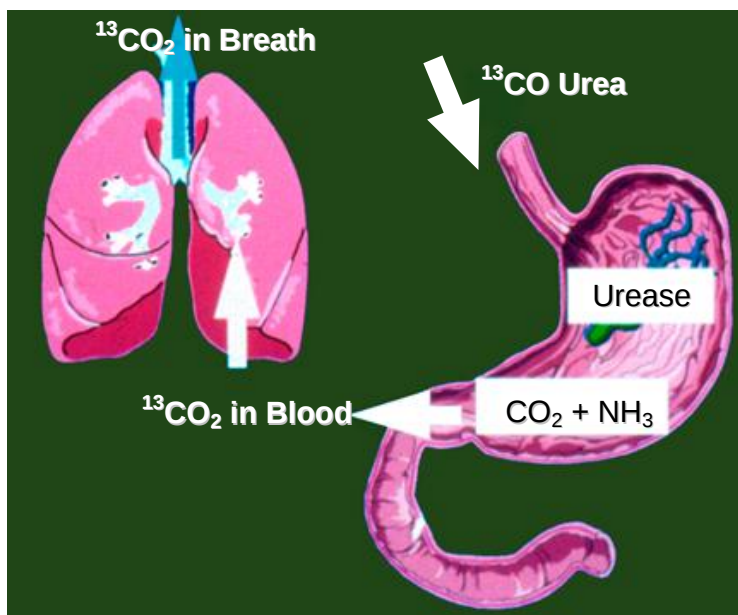
- Peptic Ulcer Disease
 - Endoscopic screening *H. pylori* -infected subjects
 - 1–6% PUD
 - Lifetime risk of developing PUD 20–40%
(4–10 times higher than *H. pylori* -negative person)
- Pathogenesis of *H. pylori* associated duodenal ulcer disease
 - Development of focal 'gastric-type' metaplasia in the duodenal bulb in response to excessive acid or extension of gastric-type mucosa across the pyloric canal into the bulb
 - Reduced bicarbonate response to acidification
 - *H. pylori* colonization → inflammation → epithelial necrosis → coalescing erosions → shut down of microcirculation → ulcer formation
- Performance Characteristics of Diagnostic tests for *H. pylori*

Test	Sensitivity (%)	Specificity (%)
○ Rapid urease test	>90	>90
○ Histology	90-98	
○ Culture	Varies widely	100
○ Urea breath test	>95	>95
○ Serology	90-100	76-96
○ Antigen-based stool assay	94	91

Useful background: Urea Breath Test to Diagnose Active infection

- [13C]-urea
 - Stable isotope
 - Non-radioactive
- [14C]-urea
 - Radioactive isotope
 - Special handling and disposal



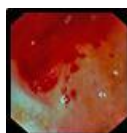
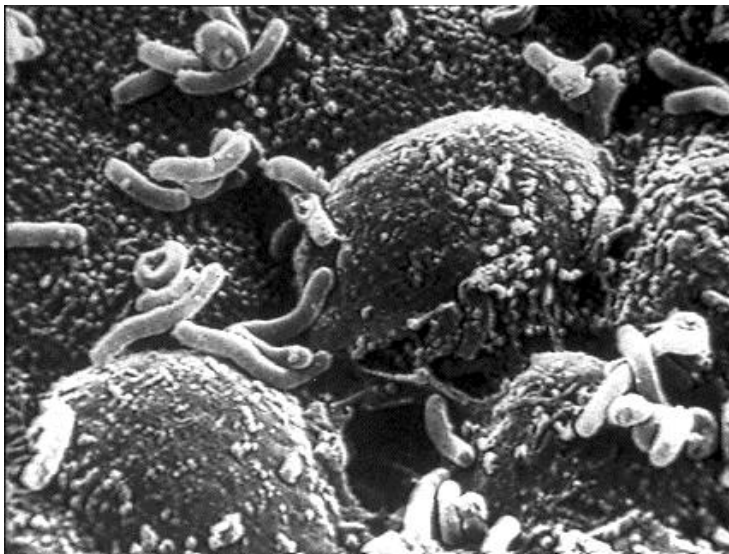


- *H. pylori* in patients with upper GI bleeding
 - Biopsies during emergency endoscopy if the patient is stable (RUT and histology)
 - If negative, serology to confirm the absence of *H. pylori*
 - If positive serology, repeat biopsies or perform UBT to confirm current infection
 - When unstable at endoscopy perform UBT later (PPI should be stopped) or take biopsies during elective endoscopy
- *H. pylori* Gastritis: reduction of risk factors after cure
 - Reduction of foveolar hyper-proliferation
 - Reduction of DNA-damaging reactive oxygen metabolites
 - Reduction of excessive iNOS-related NO production
 - Reduction of hypochlorhydria
 - Reduction of hypergastrinemia
 - Reduction of ascorbic acid hyposecretion
- Who should receive *H. pylori* Eradication therapy?
 - All users of NSAIDs, Coxibs, ASA
 - High-risk patients
 - Patients with a GU or DU

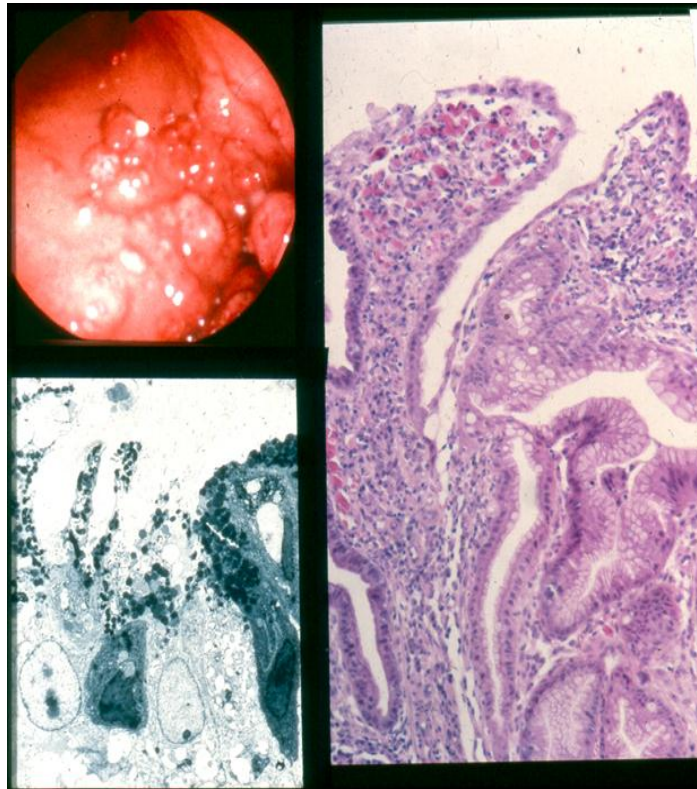


H.pylori Gastritis

- Hp-associated GI diseases
 - Acute/chronic gastritis
 - Duodenal and gastric ulcer (DU and GU) (only ~20% of Hp+ persons develop disease)
 - Accentuation of effect of smoking on PUD
 - Accentuation of ASA/NSAID effects on peptic ulcer disease (synergeneity)
 - Non-ulcer dyspepsia
 - Atrophic gastritis – intestinal metaplasia- dysplasia – GCa gastric (non-cardia)
 - Maltoma
 - Fundic gland polyps
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 - Protective against GERD
 - Halitosis
 - Carcinoid tumors (hypochlorhydria)
 - Colorectal cancer (possible association, due to hypergastrinemia)
 - Pancreatic cancer (possible)
- H. Pylori gastritis



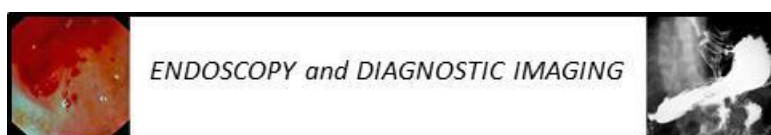
➤ H. Pylori associated gastritis



Diagnostic imaging

- H. pylori gastritis
 - Thickened folds: smooth, nodular
 - Body and antrum
- Acute erosive gastritis
 - Erosion surrounded by (halo edema)
 - Central erosion along the crest of in a rugal fold
 - Usually multiple
 - Single
 - Artifact
 - Pancreatic rest
 - GIST
 - Metastases

Differential: artifact from barium precipitate vs. punctuate “erosion”:
precipitates have no halo of edema, and are distinguishing diagnosis: not
along the crest of a rugal fold (not in line with the fold)

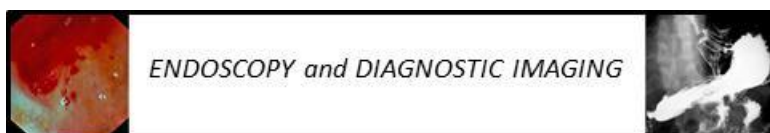


- Benign gastric ulcer
 - Round /oval ulcer crater
 - Hampton line (thin line of normal mucosa around ulcer crater)
 - Multiple in ~ 15% (multiple ulcers are likely benign)
 - Giant ulcer (> 3cm) not more likely to be malignant
 - Ulcer collar (wider, submucosa around ulcer, smooth, symmetrical collar of edematous)
 - Sump ulcer (edema around ulcer may form a mass effect around the ulcer, with sharp definition of edge with normal gastric wall, and shape that does not change with peristalsis
 - Smooth, symmetrical folds, folds run to edge of ulcer crater (ie, cross the mound of surrounding, tapered edema)
 - No nodularity / clubbing of folds
 - Ulcer extends beyond the normal gastric contour
 - Usually lesser curve
 - Benign ulcer may penetrate / fistulize form abscess / perforate pneumoperitonium
 - posterior wall, body or antrum
 - when on lower greater curve
 - ASA/NSAIDs
 - Carcinoma upper greater curve carcinoma
- Healing benign gastric ulcers
 - symmetrical or asymmetrical
 - Scar depression
 - Retraction (intramural fibrosis)

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Practice Pointers:

- NSAID-Induced Mucosal Damage
 - Topical irritant effect on epithelium (ion trapping; depletion of ATP via uncoupling of oxidative phosphorylation; decreased hydrophobicity of mucus gel layer)
 - Impairment of barrier properties – acid back diffusion
 - Suppression of prostaglandin synthesis
 - Reduction of gastric mucosal blood flow
 - Interference with repair of superficial injury
 - Interference with hemostasis
 - Interference with growth factors



➤ Deleterious Effects of NSAIDs

Membrane damage	Free phospholipids	Loss of hydrophobicity
➤ Hydrolysis phospholipids	○ Lyso platelet activating factor (PAF) ○ PAF ○ PAF-aceter	- Enhanced permeability - Ulceration
➤ Increased lipooxygenase-activity	○ Free radicals ○ Leukotriene A4 ○ Peptido-leukotriene ○ Increased LTC4-LTD4 LTE	- Membrane damage - Increased lysosomal activity - Vasoconstriction - Ischemia - Chronic inflammation
➤ Decreased cyclooxygenase activity	○ Prostaglandin deficiency	- Impaired blood flow - Impaired mucous and HCO₃ production
➤ Uncoupled oxidative phosphorylation	➤ AMP + free radical (via xanthine oxidase)	- Membrane damage - Lysosomal activation

➤ Scoring system for Drug-Induced Mucosal damage

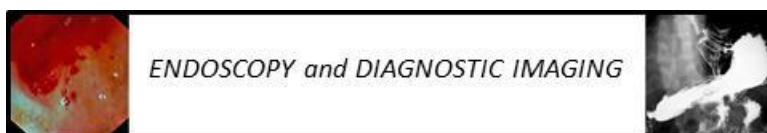
Grade 0	No visible injury
Grade 1	<10 (petechial) hemorrhages with no erosions
Grade 2	10–25 hemorrhages and/or 1–5 erosions
Grade 3	>25 hemorrhages and/or 6–10 erosions
Grade 4	>10 erosions and/or ulcer

*Grade 0-2 = clinically insignificant

**Grades 2-4 = clinically significant

➤ Drug associated gastritis-Acetylsalicylic Acid (ASA)

- Rapidly absorbed in stomach when not buffered (low pKa of 3.5; at pH 2 and 3.5, respectively 95% and 50% is protonated and fat soluble)
- Acetylsalicylic acid accumulates in surface epithelial cells due to a pH-partitioning mechanism
- Inhibits mitochondrial oxidative phosphorylation causing:
 - increased cell permeability
 - decreased secretion of mucus and bicarbonate
- Inhibits prostaglandin formation
- Destruction of barrier and back-diffusion of injurious hydrogen ions (cell shedding, erosions, disruption of microvessels)
- Tight junctions remain intact

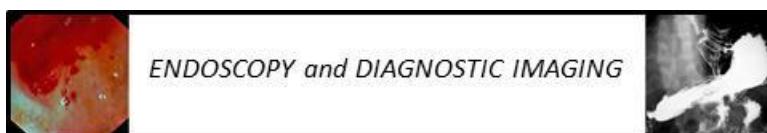


- Morning dose more damaging than evening dose, even though acidity higher in evening
- NSAID-associated GI toxicity: for the individual Patient
 - GI intolerance: up to 50% incidence
 - Endoscopic ulcers: 15-25% incidence
 - Symptomatic ulcers or ulcer complications: 2-4% /year
 - Ulcer complications: 1-2% per year
- Upper GI tract: Mucosal Damage from NSAIDs, a spectrum of injury
 - Intramucosal petechial hemorrhage
 - Superficial mucosal erosions
 - occasionally cause occult bleeding and anemia
 - Chronic ulceration
 - stomach > duodenum
 - Bleeding, perforation of ulcers
 - stomach = duodenum
- The recommendations for avoiding peptic ulcers (gastric or duodenal) associated with the use of non-steroidal anti-inflammatory drugs (NSAIDs) as a function of low, moderate and high gastrointestinal, as well as low and significant cardiovascular risk (CV) (e.g. required use of ASA plus NSAID).

	Low GI Risk	Moderate GI Risk	High GI Risk
➤ Low CV Risk (no ASA)	○ An NSAID with a low ulcerogenic potential at the lowest effective dose ○ Avoid multiple NSAIDs	○ NSAID plus PPI ○ Misoprostol ○ COXIB	○ COXIB plus PPI ○ Misoprostol
➤ Significant CV Risk (requires ASA)	○ NSAID plus a PPI	○ A combination of an NSAID and a PPI	○ Avoid NSAIDs and COXIB

Abbreviations: COXIB , COX-2 inhibitor; CV, cardiovascular risk; NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor.

Printed with permission: Lanza FL, et al. *Am J Gastroenterol* 2009; 104: pg 728-38.



Recent Updates: Gastroprotection

- Persons with cardiovascular disease (CV) may be on aspirin (ASA) when they develop a NVUGIB.
 - The reflex action may be to stop the ASA to reduce the risk of recurrent ASA-associated bleeding.
 - This is successful from the GI perspective (recurrent bleeding is higher in patients on rather than off ASA, 10.3% vs 5.4%). However this discontinuation of ASA in the high CV-risk patient leads to a higher CV mortality rate (12.9% vs 1.3%) (Sung et al., Ann. Int. Med.; 2010 152: 1-9).
 - This person with both high CV and GI risk be kept on ASA and that gastroprotective therapy with a PPI be used.
- Calculate the annual risk for an adverse effect in a 70 year old man on a high dose of NSAIDs, who has a history of a prior bleeding peptic ulcer, and is on maintenance PPI - his H. pylori status unknown.

The annual incidence of NSAID-induced adverse event can be estimated by multiplying the baseline absolute risk with patient-specific relative risk modifiers.

Risk

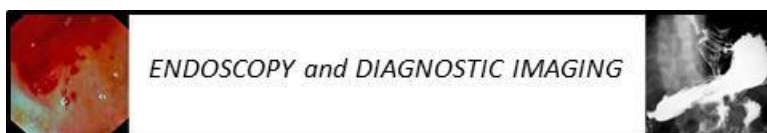
characteristic

Baseline absolute risk for GI event (%) -2.5 (1.5-4.5%)		2.5	1.5-4.5
Increase in risk [B]:	Age > 65 years	2.5	1.5-5.5
	Use of anticoagulants	2.5	2.0-5.0
	Use of steroids	2.0	1.0-3.0
	History of peptic ulcer disease	5.0	2.0-12.0
	High dose of NSAIDS	2.0	1.5-3.0
	Presence of Helicobacter pylori	1.5	1.0-3.0
Reduction in risk [C]:	Therapy with Proton pump inhibitors	0.5	

Abbreviations: NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor

Practice Pointers: Key points to consider regarding NSAIDs and gastroprotection.

- When deciding to place a patient on an NSAID, risk stratification must take into account the GI and renal risks, the presence of H. pylori, and importantly also the cardiovascular risks (Gupta and Eisen 2009).



- The use of an NSAID plus PPI, a COX-2 inhibitor, or a COX-2 inhibitor plus PPI does not prevent damage to the small or large intestine.
- The importance of cardiovascular risk of Coxibs became apparent with the APPROVE study. In the patient with both high GI and cardiovascular risk, an NSAID is given with ASA and a PPI.
- The vulnerable inflammatory phenotype of atherosclerosis is associated with a Th1 type immune response. The traditional NSAIDs and selective COX-2 inhibitors enhance this Th1 response by reducing prostanoids and promoting pro-atherogenic cytokines and plaque instability. It is proposed that this is the mechanism by which these classes of drugs enhance the cardiovascular risk (Padol and Hunt 2009; Rainsford 2010)

Adapted from: Lanza FL, et al. *AM J Gastroenterology* 2009; 104: 734.

- Concomitant PPI use reduces the risk of development of NSAID induced endoscopic lesions such as ulcers.
- Concomitant PPI use is strongly recommended for high risk NSAID users
- It is not known whether concomitant PPI use reduces the risk of clinically significant GI events such as hemorrhage and perforation
- PPI co therapy in high risk NSAID users is equivalent to COX-2 therapy in preventing NSAID induced endoscopic lesions
- PPI use is effective as secondary prevention of ulcer complications in patients needing antithrombotic therapy with aspirin or clopidogrel
- As alternatives to PPIs, misoprostol and H₂RAs can be used in the prevention of NSAID related ulcers and their complications, and their use is cost effective
- PPI co therapy is effective in the healing and prevention of recurrence of ulcers in patients maintained on long term NSAID therapy

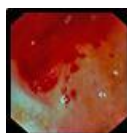
Adapted from: Arora et al. *Clinical Gastroenterology and Hepatology* 2009;7: 725-735.

Practice Pointers: Odds ratios (ORs) and *P* values for comparisons between gastroprotective strategies for persons using NSAIDs or COXIBs (COX-2 inhibitors).



A. For all upper GI complications.

NSAID + low dose misoprostol (0.74)					
NSAID + PPI (0.67)	0.88 (0.52-1.49) $P > .20$				
NSAID + PPI + low-dose misoprostol (0.58)	0.78 (0.46-1.34) $P > .20$	0.86 (0.47-1.57) $P > .20$			
COXIB (0.51)	0.68 (0.56-0.85) $P = .0006^a$	0.75 (0.53-1.06) $P = .11$	0.87 (0.52-1.49) $P > .20$		
COXIB + PPI (0.36)	0.48 (0.36-0.65) $P < .0001^a$	0.53 (0.36-0.79) $P = .0018^a$	0.62 (0.35-1.09) $P = .093$	0.70 (0.55-0.91) $P = .0068^a$	
	NSAID + low-dose misoprostol	NSAID + PPI	NSAID + PPI + low-dose misoprostol	COXIB alone	COXIB + PPI
NOTE: Those shown in bold are statistically significant.					



B. For all upper GI complications secondary to peptic ulcer disease.

NSAID + low dose misoprostol (0.61)					
NSAID + PPI (0.50)	0.81 (0.48-1.38) $P > .20$				
COXIB (0.46)	0.74 (0.55-1.00) $P = .050$	0.91 (0.55-1.50) $P > .20$			
NSAID + PPI + low-dose misoprostol (0.29)	0.46 (0.18-1.21) $P = .117$	0.58 (0.21-1.60) $P > .20$	0.63 (0.25-1.60) $P > .20$		
COXIB + PPI (0.23)	0.37 (0.23-0.57) $P < .001^a$	0.49 (0.25-0.82) $P = .0084^a$	0.50 (0.34-0.73) $P < .001^a$	0.79 (0.29-2.09) $P > .20$	
	NSAID + low-dose misoprostol	NSAID + PPI	COXIB alone	NSAID + PPI + low-dose misoprostol	COXIB + PPI
NOTE: ORs for relative risk reduction versus nsNSAID users alone shown in parentheses.					

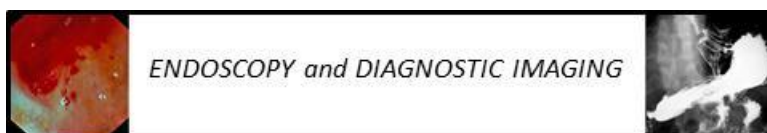
Printed with permission: Targownik LE, et al. *Gastroenterology* 2008; 134: pg. 937-44.

- The risk factors for peptic ulcer complications in patient treated with NSAIDs

➤ ESTABLISHED

○ ODDS RATIO

○ Ulcer and/or ulcer complication history	13.5
○ Age (years)	
- 60-79	3
- >70	4.2
○ NSAID dose	
- Low	2.5



- Intermediate 4.5
- High 8.6
- More toxic NSAID Variable
- Corticosteroid-associated use 10.6
- Anticoagulant-associated use 6.4
- Helicobacter pylori

➤ Who is at High Risk?

	Established	Probable	Not established
➤ Patient	Age <60 Past history	CVS disease	Sex Arthritis type
➤ Drug	High dose Toxic NSAID Steroids	1 st 3 months of treatment On warfarin	Half-life Form

➤ “The Mucosa Trial” (M=8849)

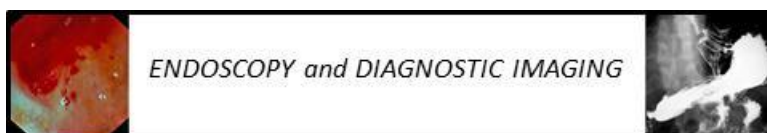
	Misoprostol	Placebo
○ Complications (HP)	25	42
○ Complication rate (%)	0.57	0.95
○ The risk of hemorrhage and perforation were reduced by approximately half by using gastroprotection with misoprostol		

➤ Phlegmonous gastritis

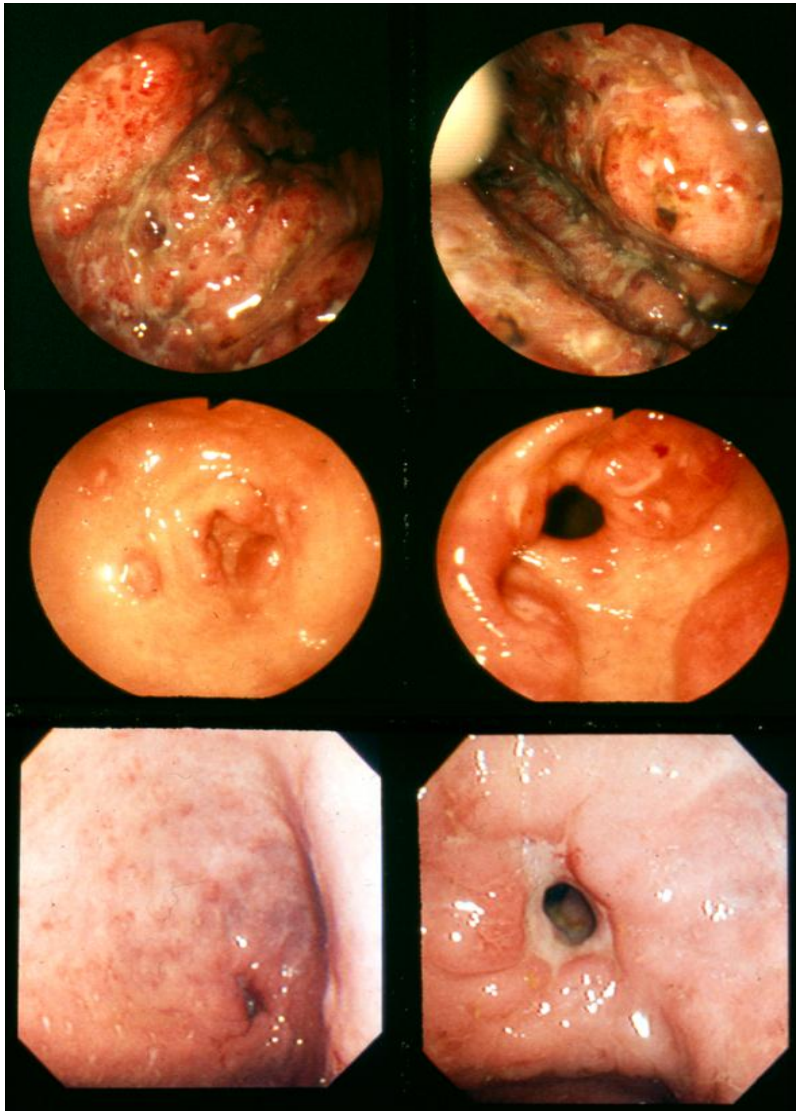
- Pg acute bacterial inflammation of mucosa and submucosa (usually hemolytic streptococci; usually prior debility, rarely prior ischemic necrosis)
- En severe erythema / exudate or erosive gastritis
- Hi severe acute gastritis
- Sy severe abdominal pain simulating an acute abdomen; purulent vomiting
- Tx broad spectrum antibiotics

➤ NSAID-induced mucosal damage

- Topical irritant effect on epithelium (ion trapping; depletion of ATP via uncoupling of oxidative phosphorylation)
- Decreased hydrophobicity of mucus gel layer
- Decreased barrier properties – acid back diffusion
- Decreased prostaglandin synthesis
- Decreased gastric mucosal blood flow
- Decreased repair of superficial injury
- Decreased hemostasis

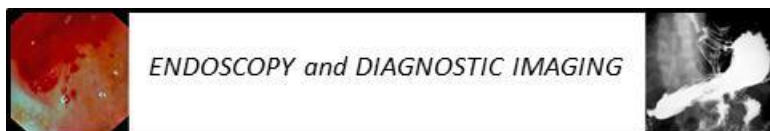


- Decreased growth factors



NON-VARICEAL UPPER INTESTINAL BLEEDING (NVUGIB)

- The patient-related adverse prognostic variables in persons with acute NVUGIB.
 - Increasing age (>60 years)
 - Increasing number of comorbid conditions (especially renal failure, liver failure, heart failure, cardiovascular disease, disseminated malignancy)
 - Shock – hypotension, tachycardia, tachypnea, oliguria on presentation



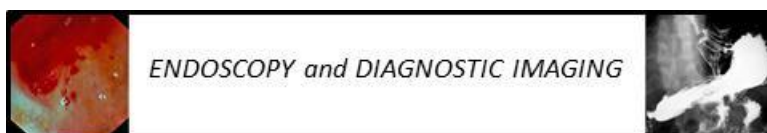
- Red blood in the emesis or stool
- Increasing number of units of blood transfused
- Onset of bleeding in the hospital
- Need for emergency surgery
- Anticoagulant use, glucocorticosteroids
- Absence of recent alcohol or drug (aspirin) intake
- Congestive heart failure
- Protruding vessel in peptic ulcer (DU or GU)
- Hematemesis, hypotension
- Varices
- Transfusion >4 units
- Malignancy

Abbreviations: NVUGIB, non-variceal upper GI bleeding ; UGIB, upper GI bleeding

- The risk Factors for peptic ulcers and bleeding
 - H. pylori
 - 70-90% in non-bleeding duodenal ulcers
 - Lower in bleeding ulcers and gastric ulcers
 - NSAIDs/ASA (dose dependant)
 - Increased risk of ulcers and bleeding with doses as low as 75mg/day with ASA
 - Corticosteroid + NSAIDs
 - Little increased risk when used alone
 - With NSAIDs increased risk for ulcer complications (X2) and GI bleeding (X10)
 - Oral anticoagulants +/- NSAIDs
 - Increased risk of bleeding vs controls: alone (-3.3), with NSAIDS (-12.7)

Practice Pointers: The Rockall Risk Score Scheme for assessing prognosis in patients with NVUGIB (PUD).

Variable	0	1	2	3
Age (years)	< 60	60-79	≥ 80	≥ 80
Shock	SBP ≥ 100, PR < 100/min	SBP ≥ 100, PR ≥ 100	SBP < 100 mm, PR ≥ 100	SBP < 100, PR ≥ 100



Comorbidity	None	None	Cardiac failure, ischemic heart disease, any major comorbidity	Renal failure, liver failure, disseminated malignancy
Diagnosis at time of endoscopy	Mallory-Weiss tear, or no lesion identified and no stigmata of recent hemorrhage	All diagnoses except malignancy	Malignancy of the upper GI tract	
Stigmata of recent hemorrhage	None, or dark spot only		Blood in upper GI tract Adherent clot Visible or spurting vessel	

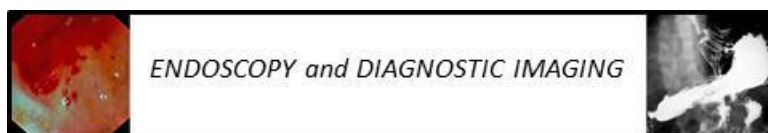
Maximum score prior to endoscopic diagnosis=7, maximum score following diagnosis=11

Abbreviations: GI, gastrointestinal; NVUGIB, non-variceal upper GI bleeding ; PUD, peptic ulcer disease; PR, pulse rate; SHR, endoscopic stigmata of recent hemorrhage; SBP, systolic blood pressure.

Adapted from: Rockall TA, et al. *Gut* 1996; 38:416; and Atkinson RJ, and Hurlston DP. *Best Practice & Research Clinical Gastroenterology* 2008; 22(2): pg. 235.

- The causes of NVUGIB (non-variceal Upper GI Bleeding)

	<u>Causes of NVUGIB</u>
➤ Esophagus	
○ Varices	5–20%
○ Esophagitis	5–10%
○ Esophageal ulcer (Barrett's epithelium)	<3%
○ Mallory-Weiss tear	5–15%
○ Neoplasm, prosthesis, vascular malformation	<5%
➤ Stomach	
○ Peptic ulcer	15–20%
○ Erosive hemorrhagic gastritis	10–20%
○ Neoplasm	<5%

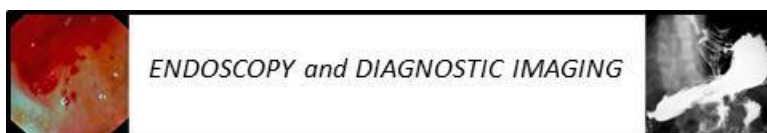


- Hiatal hernia <2%
- Vascular malformation <2%
- Duodenum
 - Peptic ulcer 20–25%
 - Stomal (anastomotic ulcer) 1–5%
 - Erosive duodenitis 5–10%
- The endoscopic hemostatic treatments (EHT) for bleeding peptic ulcer
 - Thermal Methods: contact
 - Bipolar electrocoagulation
 - Heater probe
 - Monopolar electrocoagulation
 - Thermal Methods: non-contact
 - Argon laser
 - Nd YAG laser
 - Mechanical
 - Microwave
 - Hemo clips
 - Suture (sewing machine) corkscrew
 - Band ligation
 - Injection
 - Sclerosants
 - Vasoconstrictors
 - Saline

Practice Pointers

- pH Effect on Non-variceal Upper GI Bleeding (NVUGIB)

6.7–7.0	Normal coagulation and platelet aggregation
6.4	Platelet aggregation <50%
6.0	77% of platelet aggregates dissolve in 3 min.
5.4	Platelet aggregation completely inhibited
5.0	Plasma coagulation completely inhibited
4.0	Breakdown of fibrin clot via peptic activity
- The role of Acid in Hemostasis in NVUGIB
 - Impairs clot formation



- Impairs platelet aggregation and causes disaggregation
- Accelerates clot lysis (predominantly acid-stimulated pepsin)
- May impair integrity of mucus/bicarbonate barrier

Recent Updates: Non-Variceal Upper GI Bleeding

- A methodology has been recommended for all the future RCTs in persons with nonvariceal gastrointestinal bleeding (NVUGIB) (Laine et al., 2010).
- No scoring system has been validated to use to predict when rebleeding will occur after endoscopic hemostatic therapy (El munzer et al., 2008; Ref#19). Thus it is not recommended to routinely undertake a second-look EGD. Rather, individualize such practice based on the unproven endpoints of clinically apparent recurrent bleeding, unexplained low level of hemoglobin concentration after appropriate transfusion, hemodynamic instability, multiple patient morbidities, or a high risk bleeding lesion seen at the index of EGD.
- A clinical method to estimate volume depletion in the patient with an upper GI bleed

	Class I	Class II	Class III	Class IV
○ Blood loss (mL)	<750	750-1500	1500-2000	>2000
○ Blood loss (% blood volume)	<15	15-30	30-40	>40
○ Heart (beats/min)	<100	>100	>120	>140
○ Blood pressure	Normal	Normal	Decreased	Decreased
○ Pulse pressure	Normal or increased	Decreased	Decreased	Decreased
○ Ventilatory rate (breaths/min)	14-20	20-30	30-40	>35
○ Urine output (mL/h)	>30	20-30	5-15	Negligible
○ Mental status	Slightly anxious	Mildly anxious	Anxious and confused	Confused and lethargic
○ Fluid replacement	Crystalloid	Crystalloid	Crystalloid and blood	Crystalloid and blood

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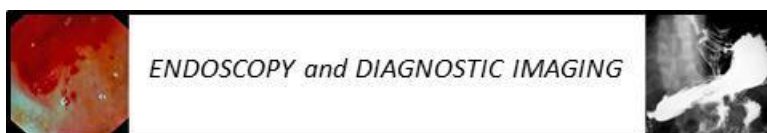
- Bleeding peptic ulcer: endoscopic management
- Proven efficacy *
 - Preventing rebleeding
 - Reducing surgery
 - Improving survival
- Most value in
 - High-risk patients
 - High-risk ulcers
- Little to choose between modalities
 - Local availability
 - Local expertise
 - Portability / ease of use
 - Ease of teaching skills
 - Cost
- The rates (%) of rebleeding, surgery and mortality, without and with endoscopic hemostatic therapy (ET), using the Forrest classification of bleeding peptic ulcers.

EGD appearance	Prevalence	Rebleeding Rate(%)		Surgery Rate (%)		Mortality rate (%)	
		No ET	ET (~70%↓)	No ET	ET (~80%↓)	No ET	ET (~50%↓)
➤ Active Bleeding (Ib, ouzing)*	18	55	20	35	7	11	<5
➤ Visible vessel (IIa); not bleeding	17	43	15	34	6	11	<5
➤ Adherent clot (IIb)	15	22	5	10	2	7	<3
➤ Flat pigmented spot (IIc)	15	10	<1	6	<1	3	<1
➤ Clean ulcer base (III)	35	<5	n/a	0.5	n/a	2	n/a

*Forrest 1a, active bleeding (spurting)

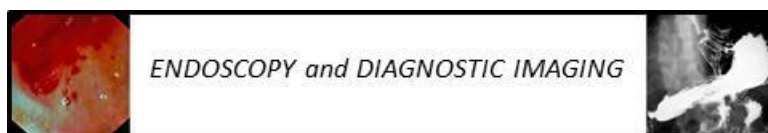
Abbreviation: ET, endoscopic hemostatic therapy

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Practice Pointers: UGIB

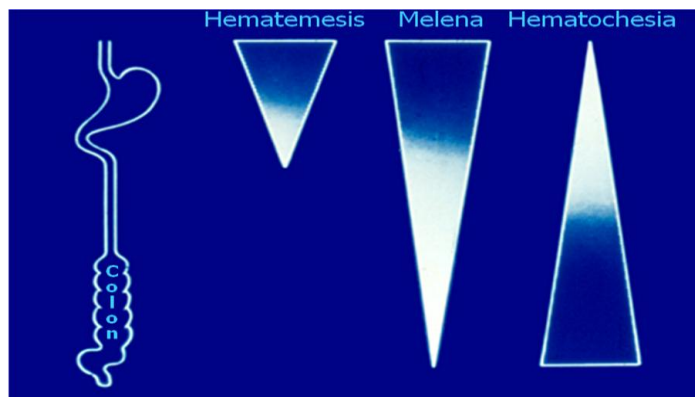
- A negative NG aspirate in the patient who presents with melena or hematochezia reduces the likelihood of an upper GI source of the bleeding, but because of curling of the tube or duodenal bleeding which does not reflux into the stomach, 15-18% of persons with an upper GI source for bleeding will have a non-bloody aspirate.
- The distribution of the endoscopic nature of bleeding ulcers is clear-based, 55%; a flat pigmented spot, 16%; a clot, 8%; a visible vessel, 8%; and active bleeding, 12% (Enestvedt BK, et al. *Gastrointest Endosc* 2008:422-9.)
- RCTs show that adding bolus plus infusion of PPI to endoscopic hemostatic therapy (EHT) significantly decreased bleeding (NNT, 12) surgery (NNT, 28) and death (NNT, 45) (Laine L, et al. *Clin Gastroenterol Hepatol* 2009:33-47).
- In the patient with UGIB due to esophageal varices (5-30% of all cases of UGIB), adding octreotide plus infusion for 2-5 days for EHT improves the control of bleeding. Also, adding ceftriaxone or quinolones reduces bacterial infection and mortality (DeFranchis R. *J Hepatol* 2005:167-76.)
- Recurrent esophageal variceal bleeding in the Child-Pugh class A or B cirrhotic, which occurs despite repeated endoscopic variceal banding or maintenance use of nonselective beta blocker may require the placement of TIPS (transjugular intrahepatic postoperative shunt) or a distal splenorenal shunt (DSRS). The reintervention rate is much lower with DSRS than TIPS (82% vs 11%, likely due to the TIPS shunt stenosis), with no difference in rebleeding, hepatic encephalopathy or death (Henderson JM, et al. *Gastroenterology* 2006:1643-51.)
- Gastric varices due to splenic vein thrombosis can be cured by splenectomy
- In the ICU patient on a mechanical ventilator, IV H₂-receptor blocker or PPI through the nasogastric tube is superior to sucralfate to reduce stress when bleeding (Cook DJ, et al. *N Engl J Med* 1998:791-7.; Conrad SA, et al. *Crit Care Med* 2005;33:760-5.
- Reducing the intragastric concentration of H⁺ reduces the adverse effects of acid and pepsin in persons with non-variceal upper gastrointestinal bleeding. Depending upon the risk of the peptic ulcer for rebleeding endoscopic hemostatic therapy (ENT) plus an order IV PPI may be indirected (Ghassemi et al. 2009).



	EHT	PPI
○ Flat spot, clean ulcer base	-	po
○ Oozing	+	po
○ Adherent clots	+	IV
○ Nonbleeding visible vessel	+	IV
○ Arterial bleeding	+	IV

Abbreviation: EHT, endoscopic hemostatic therapy; NNT, number needed to treat; TIPS, transjugular intrahepatic portosystemic shunt; UGIB, upper GI bleeding

MANIFESTATIONS OF UPPER AND LOWER GI BLEEDING



➤ Relative frequency of cases of upper GI bleeding

- Esophagus
 - Varices 5–20%
 - Esophagitis 5–10%
 - Esophageal ulcer (Barrett) <3%
 - Mallory-Weiss tear 5–15%
 - Neoplasm, prosthesis, vascular malformation <5%
- Stomach
 - Peptic ulcer 15–20%
 - Erosive hemorrhagic gastritis 10–20%
 - Neoplasm <5%
 - Hiatal hernia <2%
 - Vascular malformation (angiodysplasia, dieulafoy/aortoenterol fistula, etc) <2%



○ Duodenum		
25%	Peptic ulcer	20–
	Stomal (anastomotic ulcer)	1–5%
	(Erosive) duodenitis	5–10%

➤ Risk factors for ulcers and bleeding

Risk factor

- | | |
|-----------------------------------|--|
| ○ <i>H.pylori</i> | ○ 70-90% in non-bleeding duodenal ulcers |
| | ○ Lower in bleeding ulcers and gastric ulcers |
| ○ NSAIDs/ASA (dose dependent) | ○ Increased risk of ulcers and bleeding with doses as low as 75 mg day ASA |
| ○ Corticosteroid + NSAIDs | ○ Little increased risk when used alone |
| | ○ With NSAIDs increased risk: |
| | - Ulcer complications -2x |
| | - GI bleeding – 10x |
| ○ Oral anti-coagulants +/- NSAIDs | ○ Increased risk of bleeding vs. controls: |
| | - Alone -3.3 |
| | - With NSAIDs -12.7 |

➤ Predictors of poor outcome

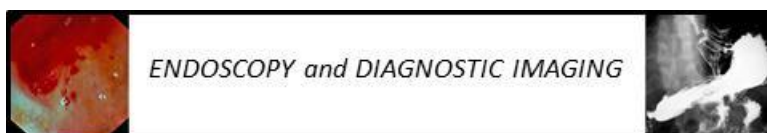
- Age over 60
- Cardiac, respiratory, hepatic or renal disease
- Absence of recent alcohol or drug (aspirin) intake
- Congestive heart failure
- Ulcer (protruding vessel)
- Hematemesis – hypotension
- Varices
- Transfusion >4 units
- Malignancy

➤ (Modified) Forrest Classification: SRH important prognostic sign

- Ia Spurting bleeding
- Ib Oozing bleeding
- IIa Non-bleeding visible vessel
- IIb Non-bleeding ulcer with adherent overlying clot
- IIc Ulcer with hematin-covered base
- III Clean ulcer base

Significant interobserver disagreement on stigmata!

Adapted from: Forrest, Lancet 1974;2:394-7.



- Role of acid in hemostasis
 - Impairs clot formation
 - impairs platelet aggregation and causes disaggregation
 - Accelerates clot lysis
 - predominantly acid-stimulated pepsin
 - May impair integrity of mucus/bicarbonate barrier

pH Effect

6.7–7	Normal coagulation and platelet aggregation
6.4	Platelet aggregation <50%
6.0	77% of platelet aggregates dissolve in 3 min.
5.4	Platelet aggregation completely inhibited
5.0	Plasma coagulation completely inhibited
4.0	Breakdown of fibrin clot via peptic activity

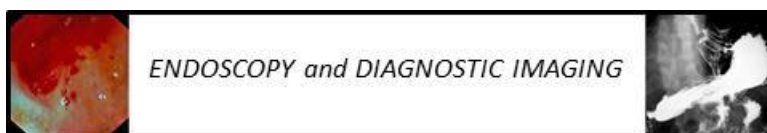
Adapted from: Patchett Gut 1989;30:1704, Green, Gastroent 1978;74:38, Low, Thromb Res 1980;17:819.

- Coagulation and *in vitro* platelet function: Influence of pH and Peptic Activity
 - At pH 6.8 - coagulation and platelet aggregation optimal
 - At pH 6.4 - doubling of coagulation times
 - reduction in platelet aggregation by 50%
 - At pH 5.4 - coagulation virtually abolished
 - platelet aggregation virtually abolished
 - Peptic activity - maximal at pH 2–3
 - virtually abolished at pH 5
 - digests clot

- (Modified) Forrest Classification of NVUGIB: Prognostic Signs
 - Ia Spurting bleeding
 - Ib Oozing bleeding
 - IIa Non-bleeding visible vessel
 - IIb Non-bleeding ulcer with adherent overlying clot
 - IIc Ulcer with hematin-covered base
 - III Clean ulcer base

Significant interobserver disagreement on stigmata!
NVUGIB, Non-Variceal Upper GI Bleeding

Adapted from: Forrest, Lancet 1974;2:394-7.



“Visible Vessel”

Discrete protuberance within the ulcer crater

Red, blue, purple : high risk
White, black: lower risk

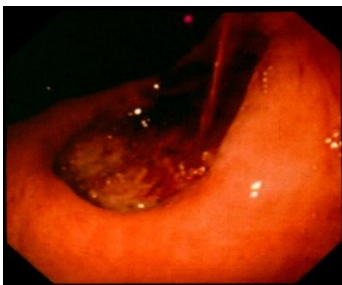
➤ Bleeding peptic ulcer: Current Endoscopic Treatments

Thermal methods: contact	Thermal methods: non-contact
○ Bipolar electrocoagulation* ○ Heater probe* ○ Monopolar electrocoagulation	○ Argon laser ○ Nd YAG laser
Mechanical	Infection*
○ Microwave ○ Hemo clips ○ Suture (sewing machine) corkscrew ○ Band ligation	○ Sclerosants ○ Vasoconstrictors ○ Saline

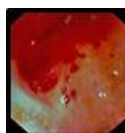
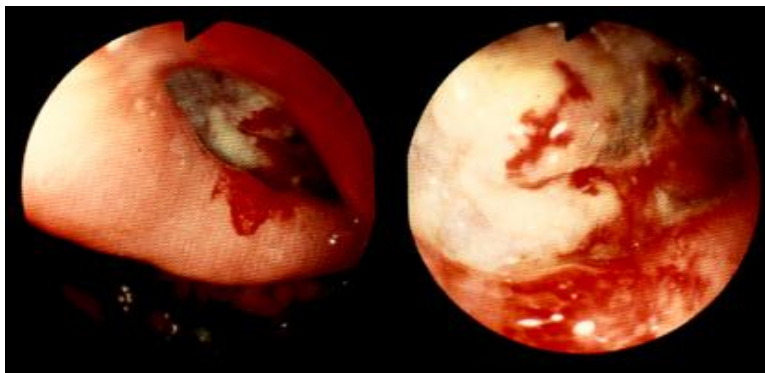
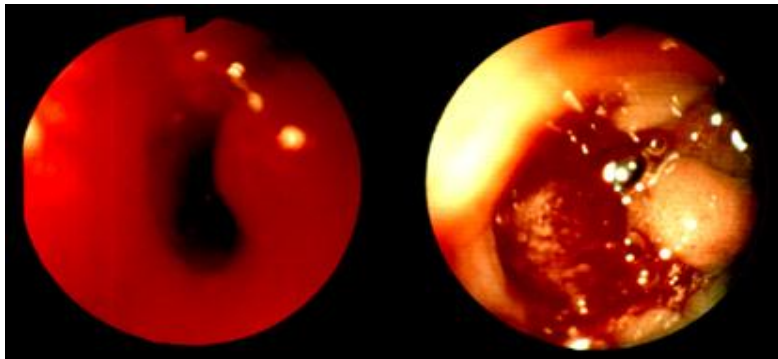
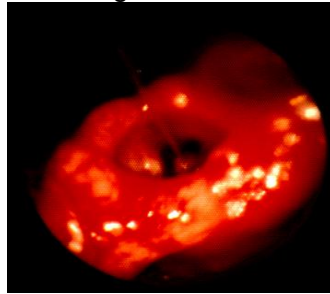
* widely used

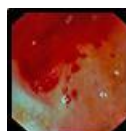
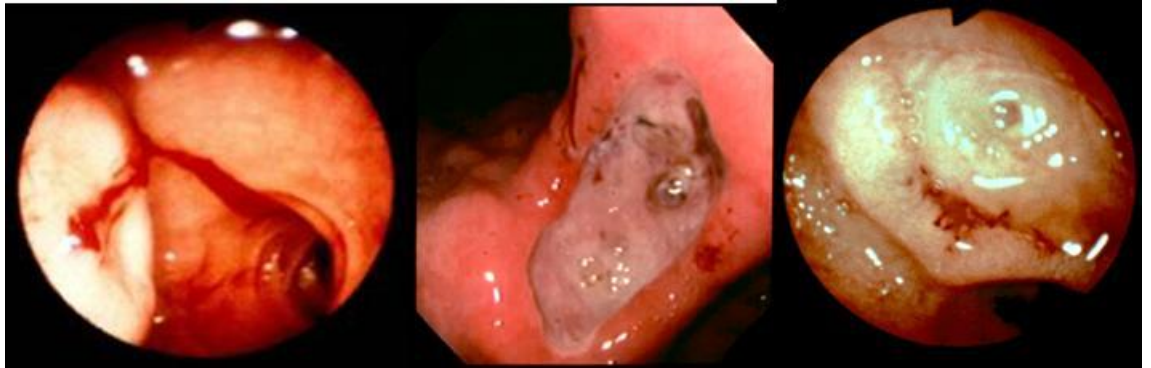
Adapted from: Wara, 1990;Laine, 1993

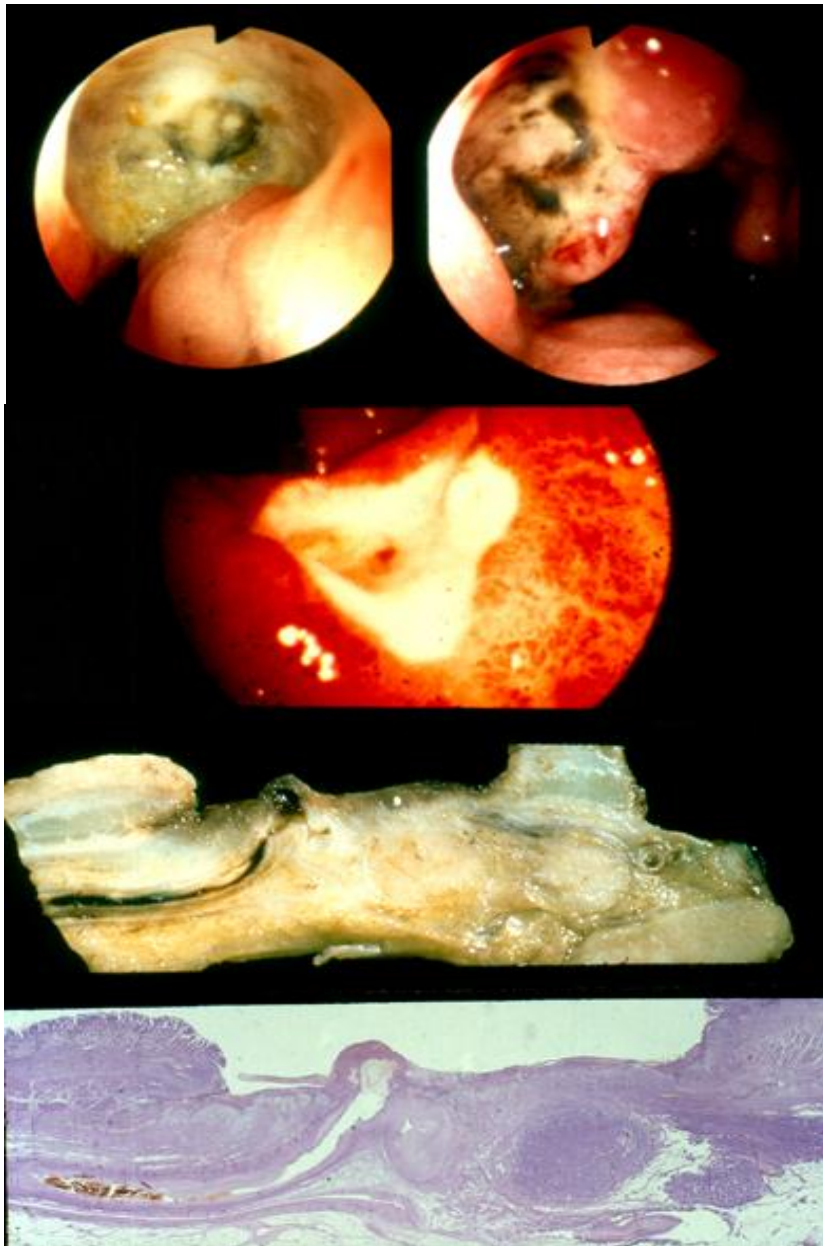
➤ Forrest I Non-Variceal Upper GI Bleeding



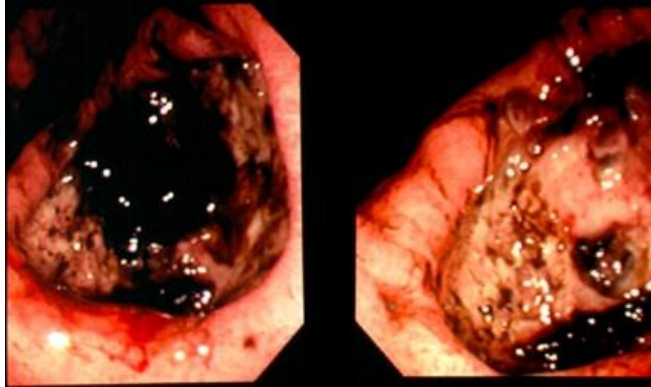
➤ Non-Variceal Upper GI Bleeding



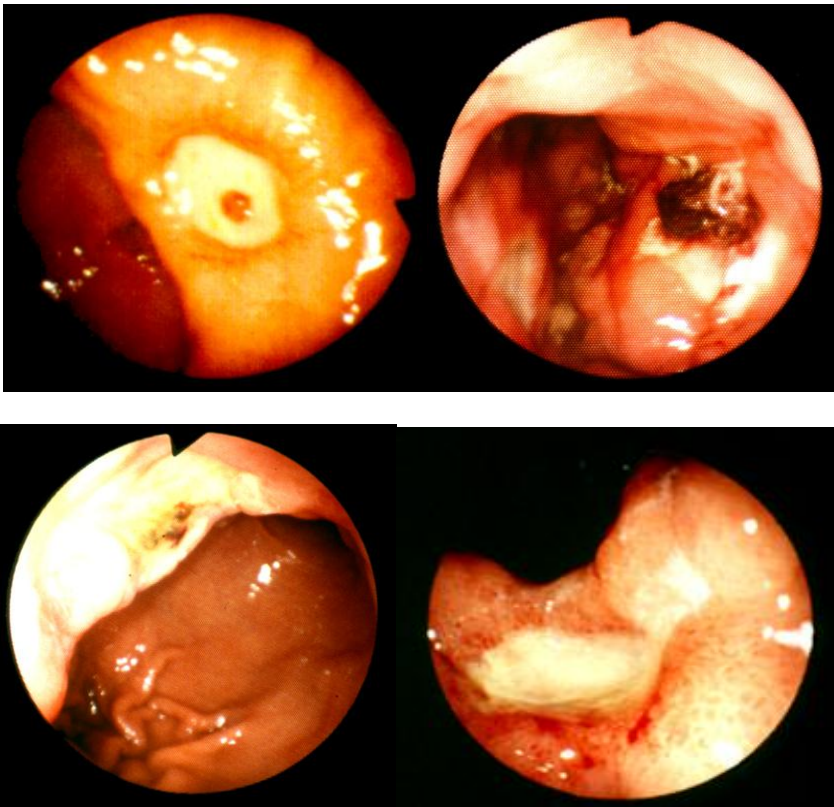


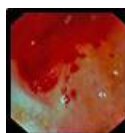
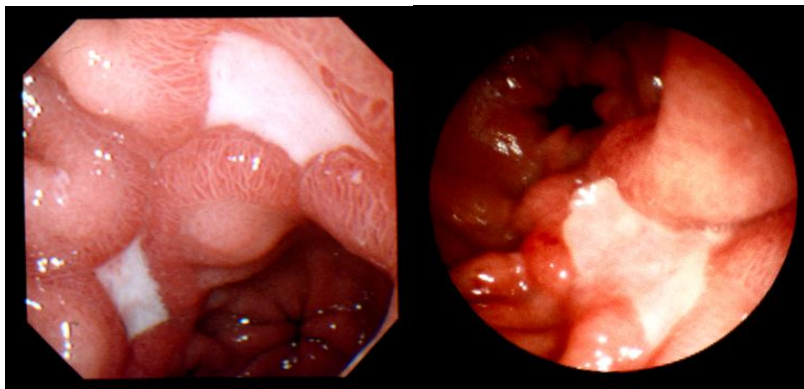
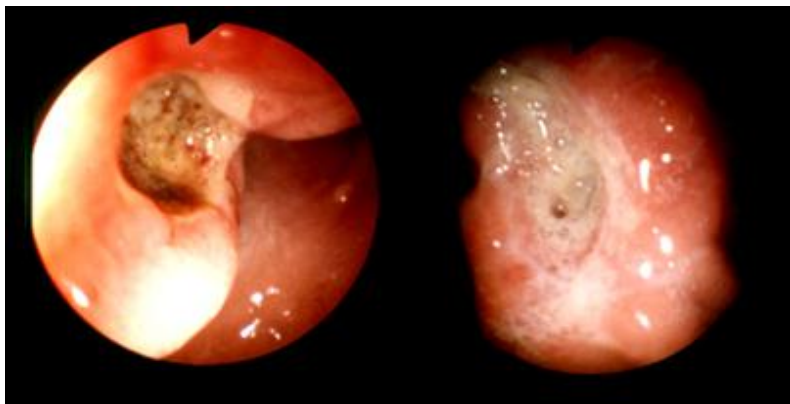
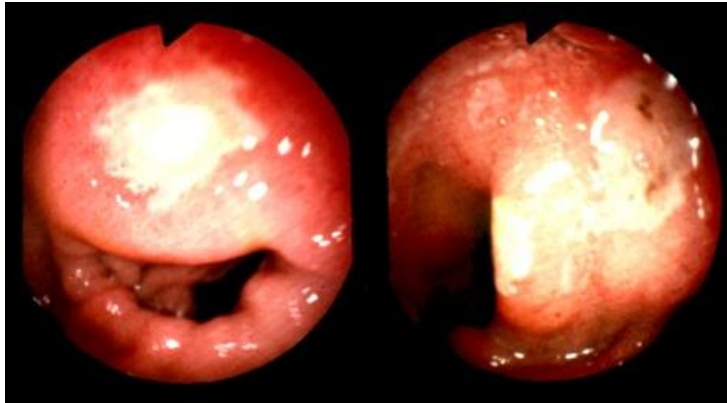


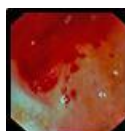
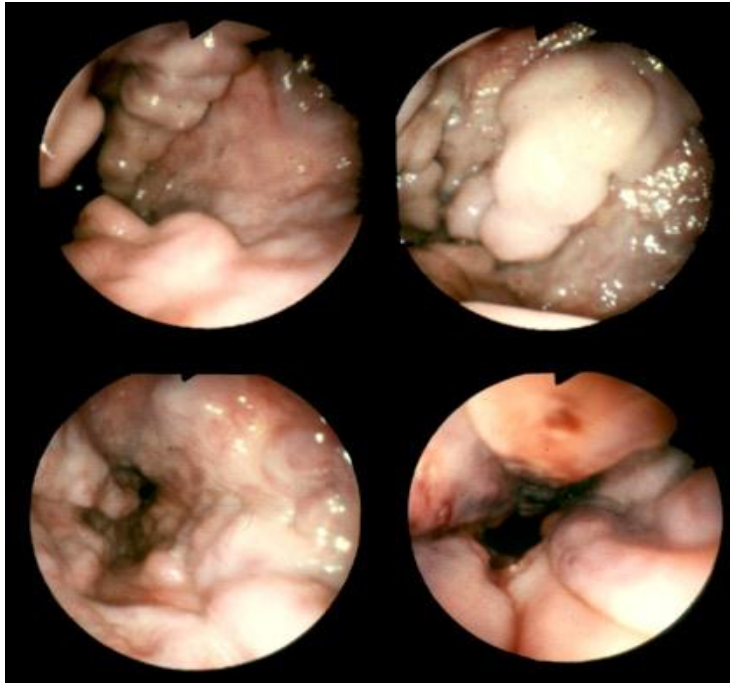


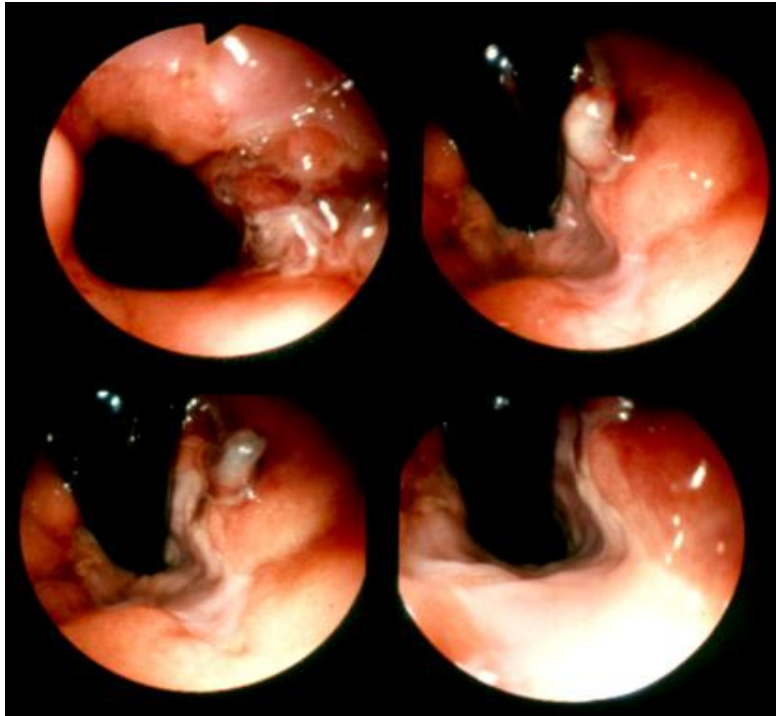


➤ Visible Vessel Gastric Ulcer









- The similarities and differences in the clinical features of NVUGIB in elderly versus younger persons.
 - Similarities
 - Presenting manifestations of bleedings: hematemesis (50%); melena (30%); hematemesis and melena (20%)
 - Peptic ulcer disease most common etiology
 - Safety and efficacy of endoscopic therapy
 - Differences (in elderly patients)
 - ↓ Antecedent symptoms (abdominal pain, dyspepsia, heartburn)
 - ↑ Prior aspirin and NSAID use
 - ↑ Presence of comorbid conditions
 - ↑ Hospitalization, rebleeding, death

Abbreviation: NVUGIB, non-variceal upper GI bleeding

Printed with permission: Yachimski PS and Friedman LS. *Nature Clinical Practice Gastroenterology & Hepatology* 2008; 5(2): pg. 81.

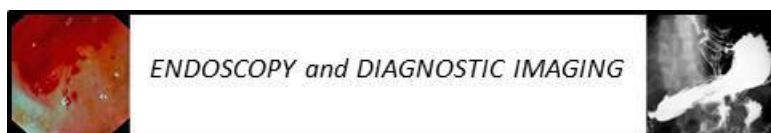
- The diagnostic methods for determining the cause of obscure GI bleeding.

Method

- Endoscopy
 - Capsule endoscopy (CE)
 - Double balloon enteroscopy (DBE)
 - Push enteroscopy (PE)
 - Intraoperative endoscopy
 - Endoscopy**
 - Colonoscopy**
- Small bowel contrast X-ray
 - Small bowel single contrast
 - Small bowel double contrast (enteroclysis)
- CT/MRI
 - CT angiography
 - CT/MRI enteroscopy
 - CT-enteroclysis
- Angiography
 - Elective (no acute bleeding)
 - With acute bleeding
- Scintigraphy
 - Erythrocyte scintigraphy (RBC scan)
 - Meckel's scintigraphy
- Video capsule endoscopy

Abbreviations: CE, capsule endoscopy; DBE, double balloon enteroscopy; EGD, esophagogastroduodenoscopy; PE, push enteroscopy

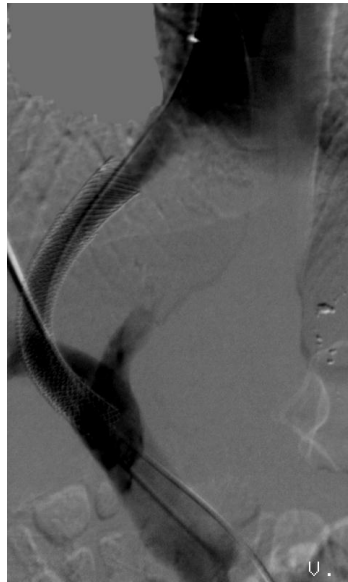
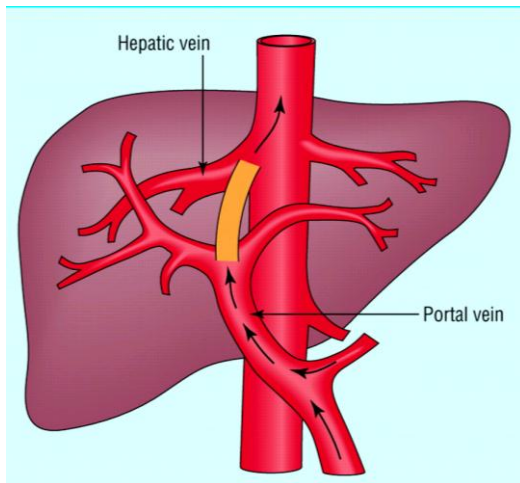
Adapted from: Heil U. and Jung M. *Best Practice & Research Clinical Gastroenterology* 2007;21(3): pg. 402.



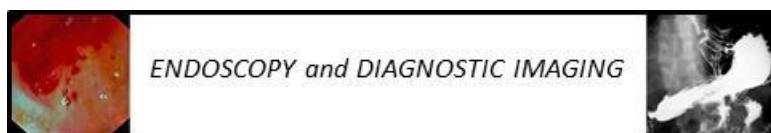
ESOPHAGEAL VARICES AND PORTAL HYPERTENSION **GASTROPATHY**

Practice Pointers:

- Transjugular intrahepatic portosystemic shunt (TIPS)



- Varices with Red Colour Signs
 - Red wale marking: dilated venule longitudinally oriented on varix surface (wale or whip mark)
 - Cherry-red spot: small red spotty venules on varix surface
 - Hematocystic spot: large round crimson red projection (>4 mm O) resembling a blood blister
 - Esophageal Variceal Bleeding – Natural History of Bleeding



- Esophageal Varices

Child class	1 month	1 year	2 years
A	<10	76	65
B	30	52	39
C	>45	35	23

- The sclerotherapy Complications for Bleeding Esophageal Varices

- Esophagus

- Ulceration
- Necrosis of esophageal wall (2–5%)
- Perforation (8-12%)
- Late fibrosis and stenosis
- Disturbed motility
- Late fibrosis and stenosis (0–53%)
- Persistent dysphagia (6%)

- Lung

- Pleural effusions

- Spinal Cord

- Pneumonia
- Spinal cord injury

- Small Bowel

- Small bowel infarction

- Infection

- Fever (2–50%)
- Bacteremia (~ 50%)
- Pleural effusion (~ 80%)

- Death

- Mortality – overall (0–13%)
– elective (1–2%)

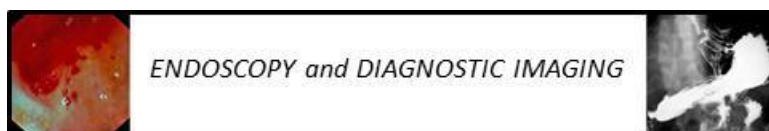
- The banding Ligation for bleeding esophageal varices of complications

- Aspiration

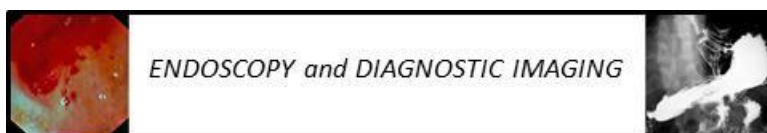
- Bleeding ulcers

- Bacteremia

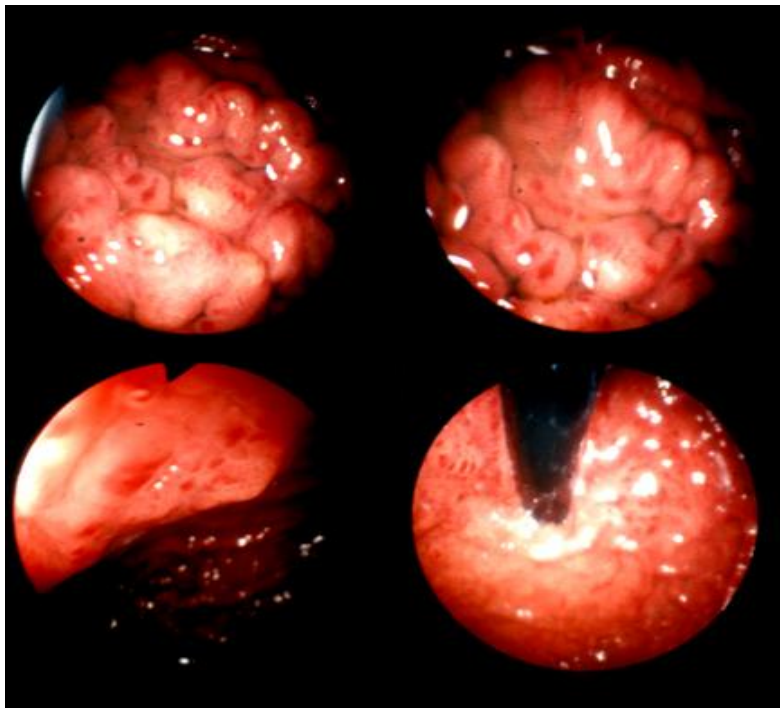
- Perforation esophagus if overtube is used



- vs Sclerotherapy
 - Equally effective (~90%)
 - More rapid variceal eradication
 - Adverse effects less frequent
 - Better survival
 - Banding is treatment of choice for bleeding esophageal varices
- The pharmacologic Agents used in the Treatment of Portal Hypertension
 - Splanchnic vasoconstrictors
 - Direct smooth muscle constrictors
 - Vasopressin
 - Terlipressin
 - Non-selective beta-adrenergic blockers
 - Propranolol
 - Nadolol
 - Timolol
 - Somatostatin receptor agonists
 - Somatostatin
 - Octreotide
 - Vasodilators
 - Nitrates
 - Alpha-adrenergic blocker
- The endoscopic appearances of congestive gastropathy
 - Mild
 - Scarlatina (fine pink speckling)
 - Moderate
 - More pronounced patchy reddening—striped appearance
 - Snake skin (quite specific)—white reticulated pattern
 - Severe
 - Cherry spots—diffuse hemorrhagic
 - Congestive gastropathy: endoscopic appearances
 - Mild – Scarlatina (fine pink speckling)
 - Moderate – More pronounced patchy reddening – striped appearance
 - Snake skin (quite specific) –
 - Severe white reticulated pattern
 - Cherry red spots – diffuse hemorrhagic



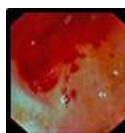
➤ Portal hypertensive gastropathy



SO YOU WANT TO BE A GASTROENTEROLOGIST!

Q. How can you attempt to differentiate between involuntary or malingering pain?

A. Try to distract patient by pretending to auscultate but pushing in the stethoscope, and watch the patient's face for signs of discomfort



ENDOSCOPY and DIAGNOSTIC IMAGING



GASTRIC POLYPS

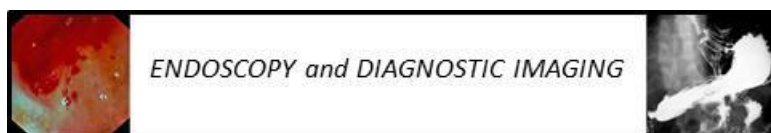
- Classification of gastric polyps: neoplasia (34%)
 - Epithelial
 - Intestinal-type adenoma
 - Tubular (17%)
 - Tubulopapillary
 - Papillary
 - Pyloric gland adenoma
 - Adenocarcinoma
 - Endocrine
 - Carcinoid tumor
 - Mesenchymal
 - Leiomyoma
 - Neurogene tumors,
 - Neurinoma, neurofibroma
 - Granular cell tumor
 - Lipoma
 - Sarcoma
 - Neurosarcoma, fibrosarcoma
 - Lymphatic
 - Mucosa associated lymphoid tissue
 - lymphoma

- Classification of gastric polyps: Tumor-like lesions (66%)

- Fundic
 - Fundic gland
 - Hyperplastic
 - Inflammatory fibroid
 - Brunner gland heterotopia
 - Pancreatic heterotopia
 - Peutz-Jeghers
 - Cronkhite-Canada
 - Juvenile polyp
- Differential diagnosis
 - Focal foveolar hyperplasia
 - Lymphatic follicles
 - Giant folds
 - Varioliform gastritis

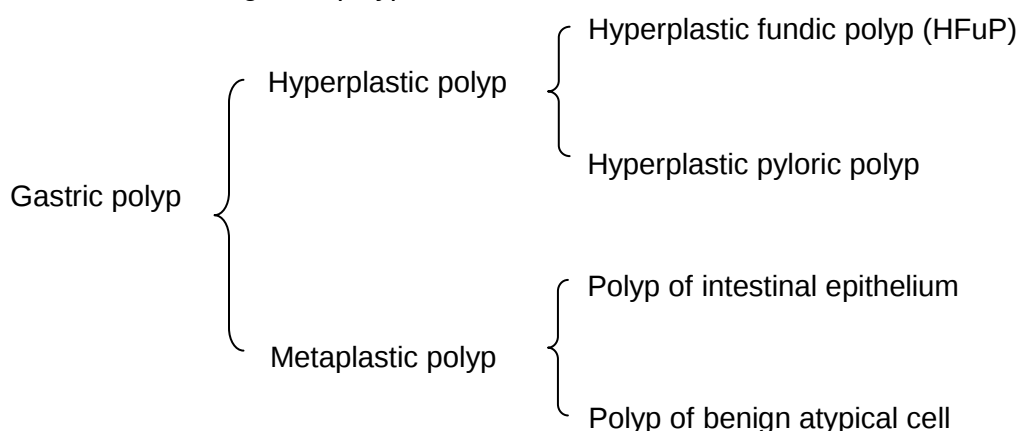
- Distribution of gastric polyps

○ Neoplasias	33.9%	○ Heterotopia	3.1%
○ Tubular adenoma	16.7%	○ Peutz-Jeghers polyp	0.6%
○ Tubulopapillary adenoma	2.2%	○ Juvenile polyp	0.3%
○ Papillary adenoma	0.2%	○ Cronkhite-Canada polyp	0.1%



○ Pyloric gland adenoma	0.4%	○ Cardia	4.4%
○ Adenocarcinoma	11.8%	○ Fundus	2.7%
○ Carcinoid tumor	2.6%	○ Corpus	49.0%
○ Tumor-like lesions	66.1%	○ Antrum	38.0%
○ Hyperplastic polyp	56.7%	○ Pylorus	2.4%
○ Inflammatory fibroid polyp	5.4%	○ Anastomosis	3.5%

➤ Classification of gastric polyps



HFuP (hyperplastic fundic polyp)

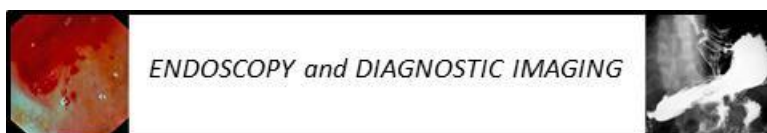
- Frequent in middle-aged female
- Originate from fundic gland region without atrophy
- Hemispheric in shape
- Multiple
- Almost the same color as the surrounding mucosa
- No elongation of foveolar epithelium
- Hyperplasia and cystic dilation of fundic gland

HFoP (hyperplastic foveolar polyp)

- Severe atrophy of fundic gland
- Pyloric antral region
- With stalk
- Single
- Red on the surface
- Marked hyperplasia of foveolar epithelium
- Formation of the gland is seldom seen
- Edematous in interstice
- Infiltration of inflammatory cells is sometimes seen

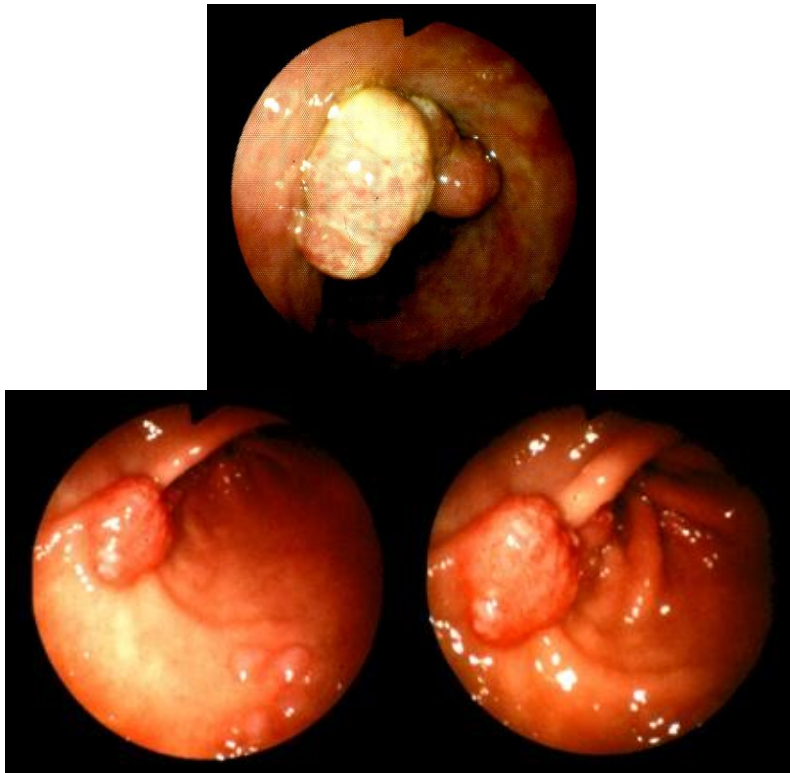
➤ Clinical situations/syndromes which can be associated with fundic gland polyps

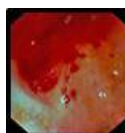
- *H. Pylori* infection
- PPI use

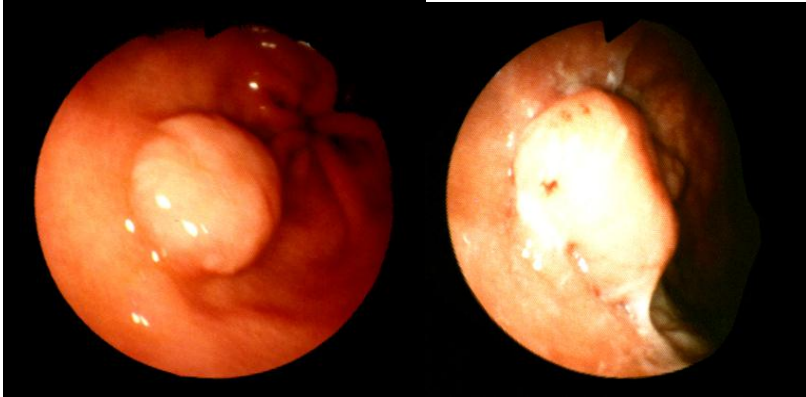


- Hypergastrinemia
- Familial adenomatous polyposis (FAP; Attenuated FAP, 0.5-1.0% lifetime risk of gastric cancer)
- Cowden's syndrome
- Idiopathic

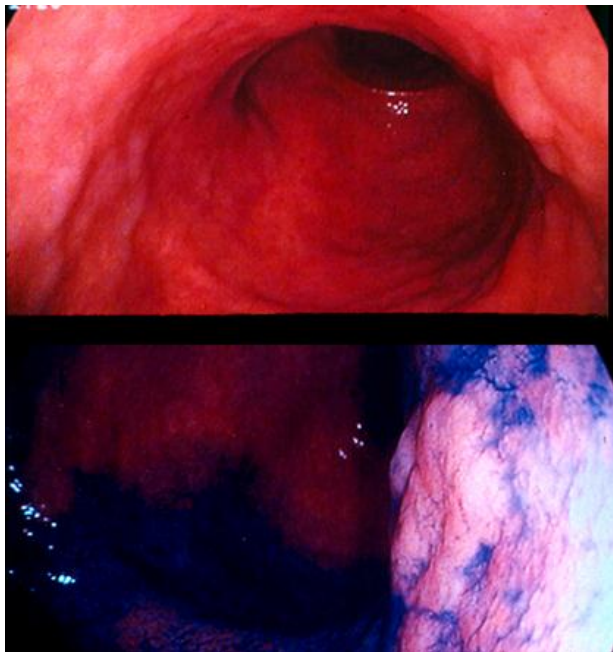
➤ Gastric polyps



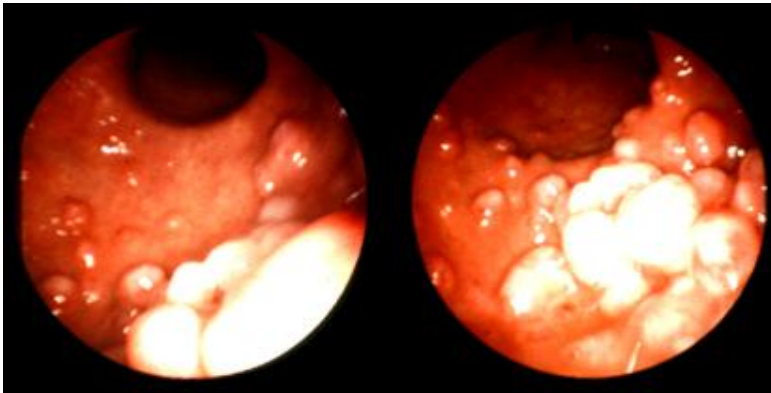




- Gastric fundic gland polyps



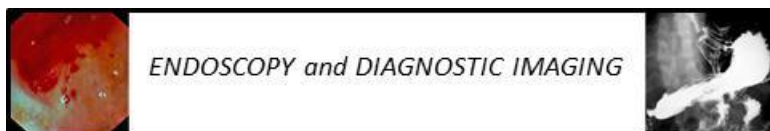
➤ Gastric Polyps



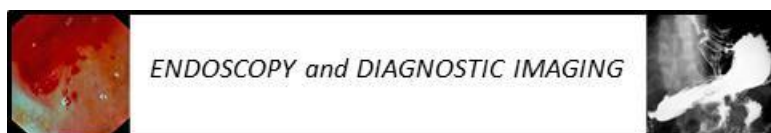
GASTRIC CANCER

Polyps

- The types of Gastric Polyps
 - Neoplasia
 - Epithelial
 - Intestinal-type adenoma
 - Tubular
 - Tubulopapillary
 - Papillary
 - Pyloric gland adenoma
 - Adenocarcinoma
 - Endocrine
 - Carcinoid tumor
 - Mesenchymal
 - Leiomyoma



- Neuroendocrine tumors
 - Neuroma, neurofibroma
 - Granular cell tumor
 - Lipoma
 - Sarcoma
 - Neurosarcoma, fibrosarcoma
- Lymphatic
 - Mucosa associated lymphoid tissue (MALT) lymphoma
- Hyperplastic fundic Polyp (HFuP)
 - Frequent in middle-aged female
 - Originate from fundic gland region without atrophy
 - Hemispheric in shape
 - Multiple
 - Almost the same color as the surrounding mucosa
 - No elongation of foveolar epithelium
 - Hyperplasia and cystic dilation of fundic gland
- Hyperplastic foveolar polyp (HFoP)
 - Severe atrophy of fundic gland
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 - Red on the surface
 - Marked hyperplasia of foveolar epithelium
 - Formation of the gland is seldom seen
 - Edematous in interstice
 - Infiltration of inflammatory cells is sometimes seen
- Tumour-like lesion
 - Fundic gland polyp
 - Hyperplastic polyp
 - Inflammatory fibroid polyp
 - Brunner gland heterotopia
 - Pancreatic heterotopia
 - Peutz-Jeghers polyp
 - Cronkhite-Canada polyp
 - Juvenile polyp
 - Metaplastic polyp
 - Polyp of intestinal epithelium
 - Polyp of benign atypical cell
- Differential Diagnosis
 - Focal foveolar hyperplasia
 - Lymphatic follicles
 - Giant folds



○ Varioliform gastritis	
Types of polyps	%
➤ Neoplasias	34
○ Tubular Adenoma	17
○ Tubulopapillary adenoma	2
○ Papillary adenoma	0.2
○ Pyloric gland adenoma	0.4
○ Adenocarcinoma	12
○ Carcinoid tumour	3
○ Tumour-like lesions	66
➤ Hyperplastic polyp	57
➤ Inflammatory fibroid polyp	5
➤ Heterotopia	3
➤ Peutz-jeghers polyp	0.6
➤ Juvenile polyp	0.3
➤ Cronkhit-Canada polyp	0.1
➤ Sites of polyps	
○ Cardia	4
○ Fundus	3
○ Corpus	49
○ Antrum	38
○ Pylorus	2
○ Anastomosis	4

- The clinical situations/syndromes which can be associated with fundic gland polyps.

- H. Pylori infection
- PPI use
- Hypergastrinemia
- Familial adenomatous polyposis (FAP; Attenuated FAP, 0.5-1.0% lifetime risk of gastric cancer)
- Cowden's syndrome
- Idiopathic



SO YOU WANT TO BE A GASTROENTEROLOGIST!

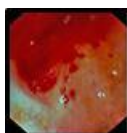
Q: What are the uses of examining the “belly button”?

- A:
- Direction of flow of blood in veins of abdominal wall—flow below umbilicus is down into saphenous veins, above umbilicus is upwards into veins of thoracic wall. In portal hypertension, dilated veins show normal direction of flow, but in IVC obstruction, flow in veins below umbilicus is reversed, i.e. Flows upward.
 - Umbilicus is common site of infiltration by cancer metastases (Sister Mary Joseph’s nodule)

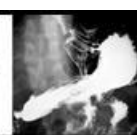
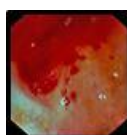
Benign Gastric Polyps

Endoscopic characteristics and pathological features for 8 types of benign gastric polyps.

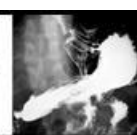
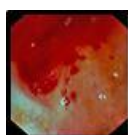
Polyp type	Location	Size	Endoscopic characteristics /appearance	Pathological features	Comments
Fundic gland (75%)	Fundus and upper body	<1 cm	○ Smooth, glassy, transparent; usually multiple polyps are found	○ <i>Helicobacter pylori</i> -associated gastritis is rare	○ Associated with PPI use, may regress ○ Dysplasia found in patients with FAP ○ Fundic gland polyp: distorted glands and microcysts lined by parietal and chief cells; no or minimal inflammation
Hyperplastic (20%)	Random, adjacent to ulcers or stoma sites, or in the cardia if related	Generally <1 cm	○ Small polyps have a smooth dome; large polyps are lobulated, and erosions are common	○ Atrophic gastritis with intestinal metaplasia ○ <i>Helicobacter pylori</i>-associated gastritis (25%), dysplasia is rare (<3%) and	○ <i>Hyperplastic</i> elongated, cystic, and distorted foveolar epithelium, marked



	to acid reflux			found in polyps <2 cm	regeneration ; stroma with inflammation , edema, and smooth muscle hyperplasia
Adenoma	<i>Incisura angularis</i> , found in the antrum than fundus	<2 cm	o Velvety, lobular surface; exophytic, sessile or pedunculated; usually solitary (82%)	- o Atrophic gastritis with intestinal metaplasia - o May be accompanied by coexistent carcinoma	o <i>Adenoma</i> dysplastic intestinal- or gastric-type epithelium with variable architecture
Inflammatory fibroid	Submucosal, found near the pyloric sphincter	Median 1.5 cm; generally <3 cm	o Single, firm, sessile, well-circumscribed , ulceration is common	- o Pernicious anemia commonly found; - o Genetic mutations are common	o CD34+ spindled stromal cells, inflammatory cells, and thin-walled vessels in a myxoid stroma
Peutz-Jeghers	Random	<1 cm	o Pedunculated with a velvety or papillary surface	- o Normal - o Risk of adenocarcinoma rare in gastric polyps	



Polyp type	Location	Size	Endoscopic characteristics/appearance	Pathological features	Comments
Juvenile	Found more in the body than in the antrum	Variable	More rounded than hyperplastic polyps; superficial erosions; multiple polyps are usually found	- Normal - Polyps may exclusively involve stomach risk of adenocarcinoma but rare in gastric polyps	
Xanthoma	Antrum, lesser curvature, prepyloric	<3 mm	Can be multiple in groups; sessile, pale-yellow nodule or plaque	- Chronic gastritis - No association with hyperlipidemia	Xanthoma aggregates of lipid-laden macrophages in the lamina propria
Pancreatic heterotopias	Antrum, prepyloric	0.2-4.0 cm	Solitary; dome-shaped with central dimple; smooth surface	- Normal - Very rare instances of associated pancreatitis, islet-cell tumors, adenocarcinoma	<i>Pancreatic heteropia</i> normal components of pancreatic parenchyma
Gastro-intestinal stromal tumor	Random, submucosal	Variable (median 6 cm)	Well-circumscribed; overlying mucosa may be ulcerated	- Normal 25% are malignant; risk of aggressive behaviour depends on size and mitotic count	CD117+, CD34+ spindle cell or epithelioid cell tumor with variable pattern, mitoses, and stroma
Carcinoid	Body and fundus	<2 cm, larger if sporadic	Hypergastrinemic lesions: firm, yellow, broad-based and multiple. Sporadic lesions: large and single	- Autoimmune atrophic gastritis with intestinal metaplasia parietal cell hyperplasia in ZES normal mucosa if lesion is sporadic - Associated with hypergastrinemia, autoimmune atrophic gastritis, ZES or MEN	<i>Carcinoid</i> nodular proliferation of neuroendocrine cells >500 µm in diameter

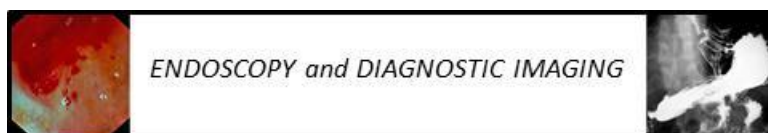


Abbreviations: FAP, familial adenomatous polyposis; MEN, multiple endocrine neoplasia; ZES, Zollinger-Ellison syndrome

Adapted from: Carmack SW, et al. *Am J Gastroenterol* 2009;104(6): 524-532.; and Carmack SW, et al. *Nat Rev Gastroenterol Hepatol* 2009;6(6): 331-341.

Diagnostic imaging

- Filling Defects
 - Benign tumors
 - Polyps
 - Fundic gland polyp
 - Hyperplastic
 - Hyperplastic, FAP
 - Adenoma
 - GIST
 - Lipoma
 - Other submucosal tumors
 - Ectopic pancreatic rest
 - Malignant tumors
 - Adenocarcinoma
 - Lymphoma
 - GIST
 - Metastases
 - Non-neoplastic
 - Fundus
 - Varices
 - Post fundoplication
 - Antrum
 - Ectopic pancreatic rest
 - Anywhere
 - Bezoar
 - Acute erosive gastritis
- Hyperplastic polyps (AKA inflammatory [chronic inflammation, mucosal proliferation, dilation of cystic glands], or regenerative, or fundic gland polyps)
 - Multiple
 - Small (< 1 cm)
 - Fundus
 - Associated with FAP (fundic gland polyposis syndrome, multiple hyperplastic polyps despite FAP polyps elsewhere being adenomas)

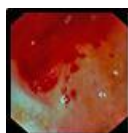


- Adenomatous polyps
 - Single usually (but may be multiple)
 - Larger (> 1 cm)
 - Antrum
 - HNPCC (Hereditary nonpolyposis colon cancer syndrome; AKA Lynch syndrome)
- Hamartomas
 - Peutz-Jeghers syndrome (PJS) – mucocutaneous pigmentation, gynecologic and gastroduodenal / colon cancer
 - Juvenile polyposis (JP)
 - Cronkhite – Canada syndrome (CCS) – skin, hair, nails and GI abnormalities
 - Cowden disease (CD) – mucocutaneous, thyroid, breast and GI abnormalities
- Benign GIST
 - Intramural
 - Intraluminal polypoid appearance
 - Well-demarcated 90° angle between mass and normal gastric wall)
 - Smooth – surfaced (typical of a submucosal tumor, with intact overlying mucosa)
 - Body
 - Similar appearance to other submucosal tumors
- Malignant GIST
 - larger
 - Irregular shape
 - Inhomogeneous
 - Intramural
 - Exophytic
 - Central necrosis
 - Fibroma
 - Neurogenic tumor
 - Vascular
 - Carcinoids

.....

Distinguishing diagnosis: central depression / ulceration

- Malignant GIST
 - Lipoma
 - Ectopic pancreatic rest (umbilication; not an ulcer, since surface is covered with normal epithelium)
 - Metastatic melanoma
-



- Lipoma
 - Single
 - Pedunculated
 - Antrum
 - Prolapsed into duodenum
 - Central ulceration
 - CT – fat
- Metastatic melanoma
 - Submucosal mass
 - Central ulceration
 - Bull's – eye (“target”) lesion
 - Multiple

.....

Distinguishing diagnosis: gastric mass with central ulceration

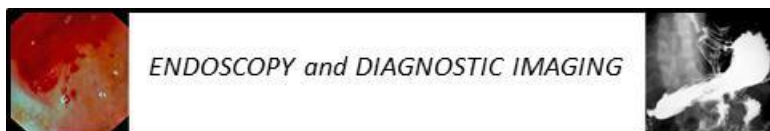
- Adenocarcinoma
 - Lymphoma
 - GIST
 - Metastatic melanoma
 - Ectopic pancreatic rest
-

- Differential diagnosis: multiple ulcers
 - ZES - benign gastric ulcers
 - Lymphoma
 - Metastatic melanoma

Gastric Cancer

Practice Pointers:

- Cause of more than ¾ million deaths annually
- Second most common fatal malignancy: 14th most common cause of death
- Changing population structure will result in increased frequency in developing world despite decrease in incidence rate
- Survival rate less than 15% at five years



Pathology	Annual risk of developing cancer	Recommended EGD/Biopsy follow-up
➤ Atrophic Gastritis	○ 0.1%	- None
➤ Intestinal Metaplasia	○ 0.25%	- 2-3 years
➤ Mild to moderate dysplasia	○ 0.6%	- 1 year
➤ Severe dysplasia	○ 6.0%	- Definitive therapy (EMR)

Abbreviation: EGD, esophagogastroduodenoscopy

Adapted from: De Vries AC, et al. *Gastroenterology* 2008;134:945-52.

➤ Unusual Presentations of Gastric Cancer

- Achalasia
- Silent jaundice
- Skin metastases
- Intestinal obstruction
- Fistula and perforation
- Duodenal spread
- Early gastric cancer

Practice Pointers: Diagnostic Imaging and Characteristics of Gastric Ulcer

➤ Benign

- Smooth border and punched out crater
- Surroundings edematous or later fibrotic
- Ulcer crater round or oval
- Crater covered by clean, smooth fibrinoid material
- Mucosa folds radiating till the crater and ending at the rim
- Ulcer rim soft or firm elastic upon biopsy
- Moving upon peristalsis if ulcer is small
- Surrounding mucosa evenly inflamed

➤ Malignant

- Irregular rim with stepformation to the crater
- Irregular ulcer crater
- Crater covered by 'dirty' necrotic material
- Mucosa folds ending abruptly away from the rim
- Folds in vicinity of the ulcer broader, narrower, abruptly ending, different in colour
- Ulcer rim elastic / firm upon biopsy
- Ulcer area often rigid without pliability upon peristalsis
- Surrounded by irregular mucosal defects or nodular elevation



- Infiltration (thick gastric folds seen on an upper GI series or EGD)
 - Folds not actually thickened (barium study is wrong – ie. varices)
 - Malignant – adenocarcinoma, lymphoma
 - Benign infiltration -granulomas:e.g. sarcoidosis, TB, Crohn's severe gastritis (ethanol, H. pylori), Menetriers disease (hyperplasia) eosinophilic gastritis
 - Multiple gastric polyps (HNPCC, FAP, fundic glands)
 - Hypersecretion (Zollinger-Ellison Syndrome)
 - Fundal varices
 - Worms

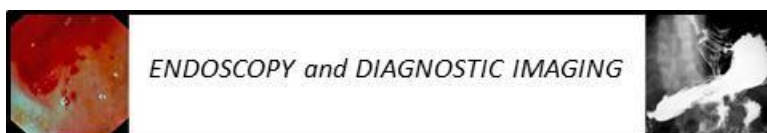
Abbreviations: EGD, esophagogastroduodenoscopy; FAP, familial adenomatous polyposis; GI, gastrointestinal; TB, tuberculosis

- The risk factors associated with the development of gastric adenocarcinoma.
 - Genetic--First degree relative with gastric cancer (hereditary diffuse gastric cancer) (2-3 fold increased risk): with mutations in E-cadherin CDH1 gene
 - HNPCC >> APC
 - Polyps--adenomatous gastric polyps (HNPCC, APC), Peutz-Jeghers syndrome, hamartomas, Menetrier's syndrome
 - *Gastric atrophy*--*H.pylori* infection, pernicious anemia, chronic atrophic gastritis, subtotal surgical resection with vagotomy for benign gastric ulcer disease
 - Diet-- salted, pickled or smoked foods, low intake of fruits and vegetables
 - Life Style--Smoking (EtOH is not an independent risk factor)
 - Esophageal --Barrett's esophagus (cancer of cardia)
 - Ménétrier disease
 - Late onset hypogammaglobulinemia
 - Intestinal metaplasia, type III

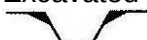
Abbreviation: HNPCC, hereditary nonpolyposis colon cancer

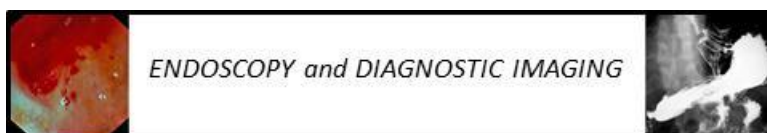
Adapted from: Houghton JM and Wang TC. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/ Diagnosis/Management* 2006: pg 1149.

What is “the best”? the “best four clinical tests for the presence of peritonitis are: rigidity, guarding, rebound and percussion tenderness.



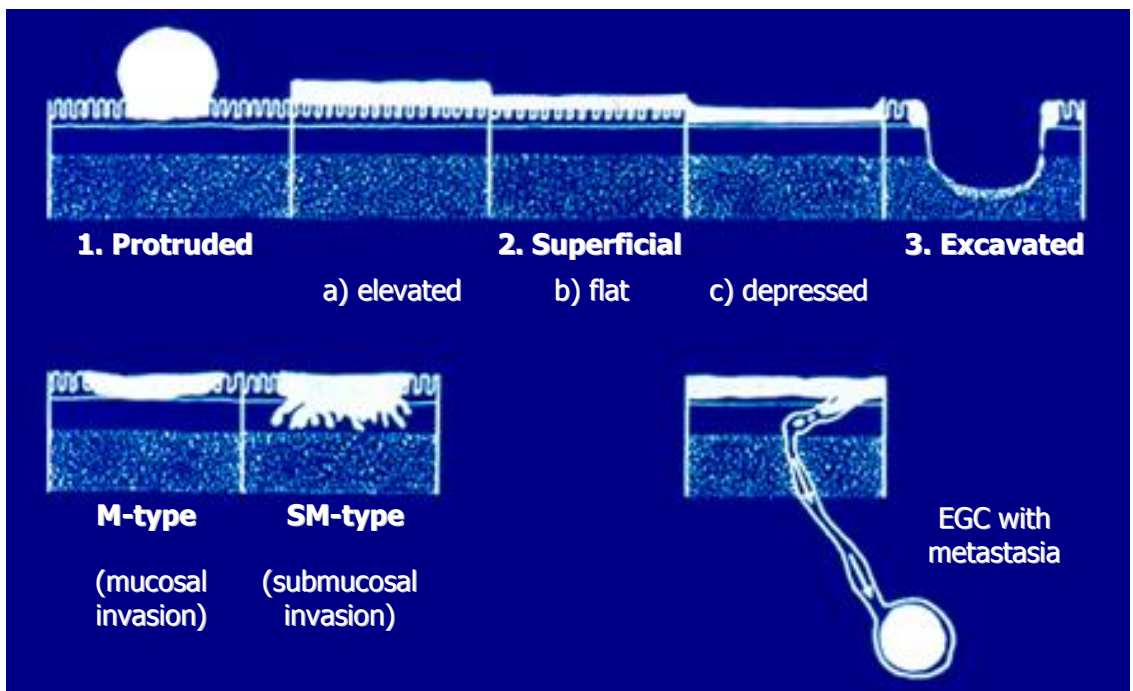
Useful background: Macroscopic types of gastric cancer.

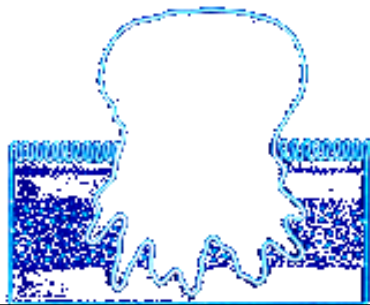
Type	Japanese classification	Paris classification
0	Superficial, flat tumors with or without minimal elevation or depression	Superficial polypoid, flat/depressed, or excavated tumors
0I	Protruded 	Polypoid
0IIa	Superficial and elevated 	Non-polypoid and nonexcavated, slightly elevated
0IIb	Flat 	Non-polypoid and nonexcavated, completely flat
0IIc	Superficial and depressed 	
0III	Excavated 	Non-polypoid and nonexcavated, slightly depressed without ulcer
1	Polypoid tumors that are sharply demarcated from the surrounding mucosa and are usually attached on a wide base	Nonpolypoid with a frank ulcer
2	Ulcerated carcinomas that have sharply demarcated and raised margins	Polypoid carcinomas that are usually attached on a wide base
3	Ulcerated carcinomas that have no definite limits and infiltrate into the surrounding wall	Ulcerated carcinomas that have sharply demarcated and raised margins
4	Diffusely infiltrating carcinomas in which ulceration is not usually a marked feature	Ulcerated, infiltrating carcinomas that have no definite limits
5	Carcinomas that cannot be classified into any of the above types	Nonulcerated, diffusely infiltrating carcinomas Unclassifiable advanced carcinomas



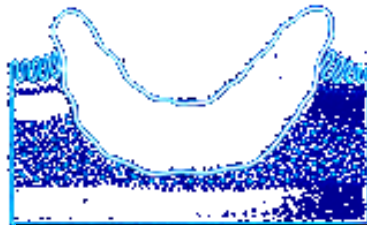
According to Japanese classification of gastric carcinoma, for the combined superficial types, the type occupying the largest area should be described first, followed by the next type (e.g. IIc+III). Types 0 I and 0 IIa are distinguished from each other by lesion thickness: type 0 I lesions have thickness more than twice that of the normal mucosa and type 0 IIa lesions have a thickness up to twice that of the normal mucosa and type 0 IIc lesions have a thickness up to twice that of the normal mucosa. Modified from data presented in the Japanese classification of gastric carcinoma and the Paris endoscopic classification of superficial neoplastic lesions.

Printed with permission: Yamamoto H. *Nature Clinical Practice Gastroenterology & Hepatology* 2007;4(9): pg. 513.





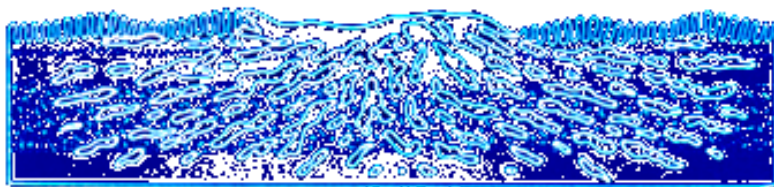
Type I: polypoid fungating



Type II: ulcerative with elevated, distinct borders



Type III: ulcerative with indistinct borders

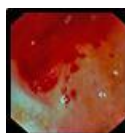


Type IV: diffuse, indistinct borders

Basic types				
Type I			Protruded Superficial	Elevated type
Type II	II a		Elevated	
	II b		Flat	Depressed type
	II c		Depressed	
Type III			Excavated	

Combined types

I + II a



ENDOSCOPY AND DIAGNOSTIC IMAGING



II a + II C

II C + III

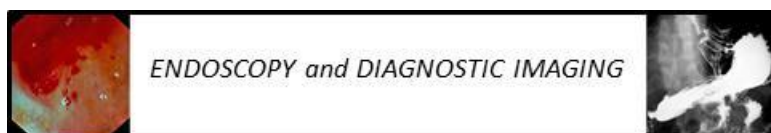
Tumors found in patients with multiple endocrine neoplasia-type I (MEN-1), and their approximate frequency % is shown for interest.

Tumors	Approximate frequency (%)
○ Parathyroid	78-97
○ Pancreatic endocrine tumor	81-82
- Gastrinoma	54
- Insulinoma	21
- Glucagonoma	3
- VIPoma	1
○ Pituitary tumors	21-65
- Prolactin-secreting	15-46
- Growth-hormone secreting	6-20
- Cushing's syndrome	16
○ Adrenal cortical adenoma	27-36
○ Thyroid adenoma	5-30

- Prevention of Gastric Cancer

- Type I (Precancerous conditions)

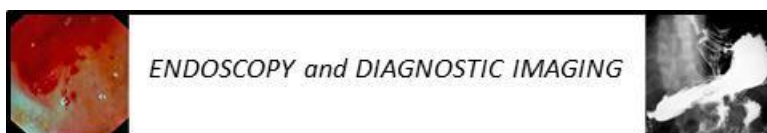
- *H. pylori* chronic gastritis with atrophy (RR: up to 9)
- Autoimmune chronic gastritis with atrophy/pernicious anemia (RR: 1-5)
- Postgastrectomy stomach (RR: 1.6 BII, 1.2 BI)
- Adenomatous gastric polyps
- Ménétrier-type hypertrophic gastritis
- Long-term drug-induced a (hypo) chlorhydria (bacterial overgrowth – nitrate reductase – ability to catalyse N-nitrosation)
- A (hypo) gammaglobulinemia



- Type II (Precancerous conditions)
 - Chronic atrophic gastritis (RR: 18)
 - Intestinal metaplasia, esp. the incomplete sulphomucin secreting subtype III (high-grade dysplasia develops into GCA in up to 85%)
 - Adenomatous polyp (10% focal malignancy)
- The palliation of gastric cancer
 - Obstruction
 - Resection
 - Proximal tumour (prothesis/radiotherapy)
 - Distal tumour (bypass/side-to-side antecolic gastroenterostomy)
 - Dysphagia
 - Radiotherapy
 - Bleeding
 - Radiotherapy
 - Endoscopic palliation (injection necrotising agents, laser, etc)
 - Best supportive care
 - Pain
 - Analgesics
 - Radiotherapy
- Compare and contrast the intestinal with the diffuse type of gastric cancer.

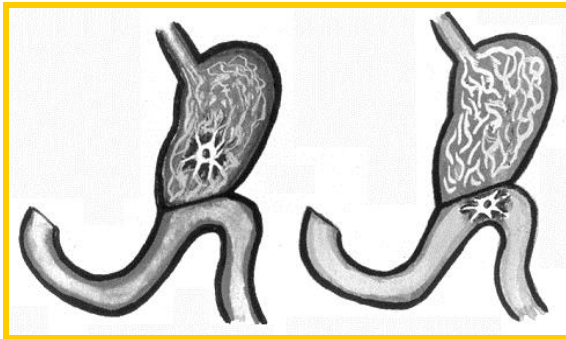
Intestinal vs Diffuse Type

Characteristic	Intestinal	Diffuse Type
➤ Clinical	○ Comparable	- Comparable
➤ Morphology	○ Cohesion, tubular structures	- Loss of cohesion - Signet ring cells
➤ Epidemiology	○ High-risk areas	- Low-risk areas
➤ Pathogenesis	○ Precursor lesions	
➤ Molecular Profile	○ Depending on the studied population	- Type of alteration partly similar



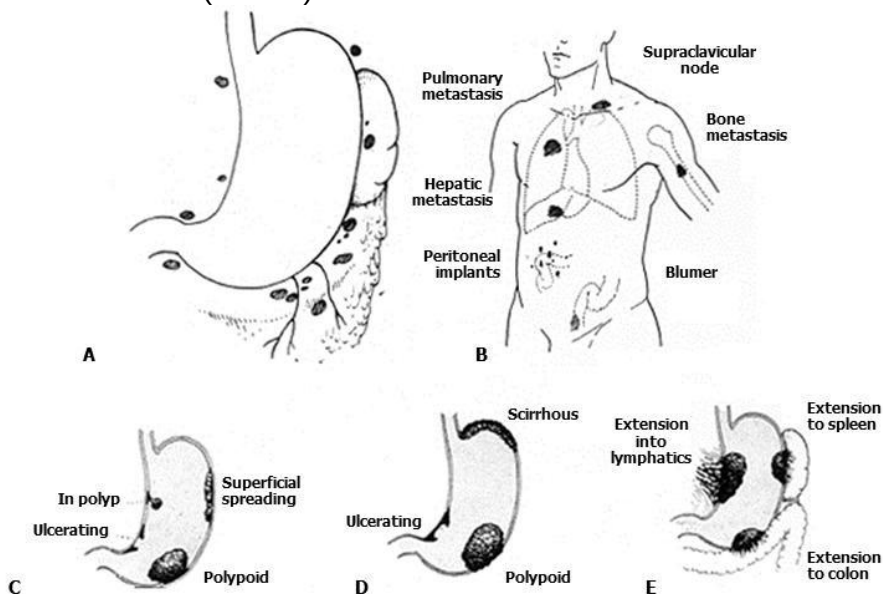
Gastric Stump Carcinoma

Stomach Ulcers following Gastric Resection

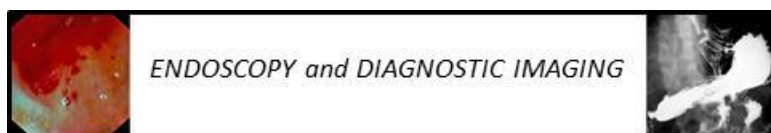


Overall incidence of cancer in gastric remnant, 3.6–15.1%

- Amsterdam Survey
 - Death due to stump cancer in 960 old gastrectomy patients >3.2%
 - Cancer rate detected by prospective endoscopic screening of 535 asymptomatic gastrectomy patients (>15 years) 4.1%
- The common sites for metastasis of gastric cancer
 - Liver
 - Lung
 - Supraclavicular lymphnodes
 - Distant abdominal lymphnodes
 - Peritoneum (ascites)



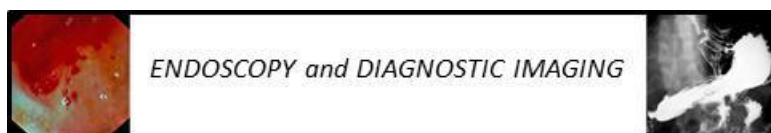
- Gastric cancer in the 2000s
 - Cause of more than ¾ million deaths annually



- Second most common fatal malignancy: 14th most common cause of death
- Changing population structure will result in increased frequency in developing world despite decrease in incidence rate
- Survival rate less than 15% at five years

Adapted from: After Murray and Lopez 1997.

- Pathological conditions associated with gastric cancer
 - Adenomatous gastric polyps (10% focal malignancy)
 - Chronic atrophic gastritis (RR: 18)
 - *H. pylori* gastritis with atrophy (RR ~ 5)
 - Gastric remnant (RR ~ 1.4)
 - Pernicious anemia (RR ~ 3)
 - Ménétrier disease
 - Late onset hypogammaglobulinemia
 - Intestinal metaplasia, type III (Incomplete sulphomucin secreting type)
 - HED → GCA in 85%
- Prevention of gastric cancer I: Precancerous Conditions:
 - *H. pylori* chronic gastritis with atrophy (RR: up to 9)
 - Autoimmune chronic gastritis with atrophy/pernicious anemia (RR: 1–5)
 - Postgastrectomy stomach (RR: 1.6 BII, 1.2 BI); overall >4% in 15 yrs)
 - Adenomatous gastric polyps
 - Ménétrier-type hypertrophic gastritis
 - Long-term drug-induced a(hypo)chlorhydria
 - A(hypo)gammaglobulinemia
- Prevention of gastric cancer II: Precancerous Lesions:
 - Chronic atrophic gastritis (RR: 18)
 - Intestinal metaplasia, esp. the incomplete sulphomucin secreting subtype III (high-grade dysplasia develops into GCA in up to 85%)
 - Adenomatous polyp (10% focal malignancy)
- Laurén classification of gastric carcinoma
 - Intestinal type
 - Diffuse type
 - Unclassified (mixed) type



	Intestinal Type	Diffuse Type
➤ Epidemiology	○ High-risk areas	– Low-risk areas
➤ Pathogenesis	○ Precursor lesions identified	
➤ Morphology	○ Cohesion ○ Tubular structures	– Loss of cohesion – Signet ring cells
➤ Molecular Profile	○ Depending on the studied population	– Type of alteration partly similar

➤ Comparison of benign vs. malignant gastric ulcer

- Smooth border and punched out crater
- Surroundings edematous or later fibrotic
- Ulcer crater round or oval
- Crater covered by clean, smooth fibrinoid material
- Mucosa folds radiating till the crater and ending at the rim
- Ulcer rim soft or firm elastic upon biopsy
- Moving upon peristalsis if ulcer is small
- Surrounding mucosa evenly inflamed

➤ Comparison of malignant vs. benign gastric ulcer

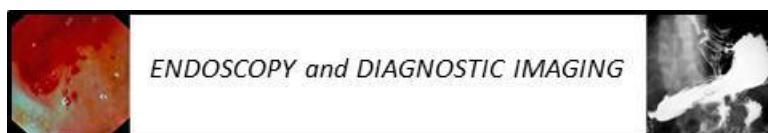
- Irregular rim with stepformation to the crater
- Irregular ulcer crater
- Crater covered by 'dirty' necrotic material
- Mucosa folds ending abruptly away from the rim
- Folds in vicinity of the ulcer broader, narrower, abruptly ending, different in color
- Ulcer rim elastic / firm upon biopsy
- Ulcer area often rigid without pliability upon peristalsis
- Surrounded by irregular mucosal defects or nodular elevation

Diagnostic imaging

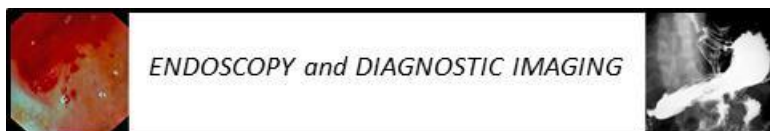
- Adenocarcinoma

➤ Ulcer

- Ulcerating mass
- Lobulated contour of mass
- Irregular surface (mucosa – based lesions)
- Nodular orifice and floor of ulcer
- Tissue around ulcer is nodular



- Tissue around ulcer stops suddenly with an acute angle to the normal gastric tissue
- Ulcer crater does not project beyond the expected location of the gastric wall
- Ulcer is placed asymmetrically in the surrounding tissue
- Ulcer is wider than deep (width > depth)
- Converging folds
 - Clubbed
 - Fused
 - Tapered
 - Amputated
 - Stop before the ulcer crater
 - Lack of mucosal markings (gastric folds) usually indicates ulceration
- Carman meniscus sign
 - Lesser curve malignant ulcer
 - Nodular tissue around ulcer
 - Compression of both sides nodular surrounding tumor produces a half-moon, crescent shape (pathognomic for adenocarcinoma)
 - Usually single
- Infiltrative scirrhus tumor
 - Narrowing of stomach ("leather bottle")
 - Mucosa nodular
 - Ulceration
 - Thick walls of fundus / body
 - Contour of stomach is irregular, scalloped
 - Stomach not distensible
 - Long segment, with intact folds
- Metastatic gastric cancer
 - Serosal contours of gastric wall are irregular / fuzzy
 - CT thickened wall
 - Lymphadenopathy
 - Para-pancreatic
 - Para-aortic
 - Para middle colic artery
 - Soft tissue masses
 - Spread to perigastric, omentum, peritoneum
 - Below renal pedicles:
 - Ovary (krukenberg tumor)
 - Pancreas
 - Liver



➤ Lymphoma

- May be solitary, or multiple masses
- Mass
 - Ulcerative
 - Infiltration
 - Polypoid
 - Intraluminal fungating
- May narrow stomach by infiltration
- May be localized or extensive
- Nodules (stomach; duodenum [crosses the pylorus])
- Infiltration of submucosa
- Body of stomach
 - Remains distendable (compliant)
 - No narrowing of lumen
- Thickened folds

CT lymphadenopathy perigastric not below renal pedicles

Distinguishing diagnosis: lymphoma / adenocarcinoma

	Lymphoma	Adenocarcinoma
Number	Single or multiple	Single
Extent	Extensive	Localized
Origin	Submucosa	Mucosa
Crosses pylorus	Yes	No
Narrowed lumen	No	Yes
Distensible	Yes	No
Disorganized	Yes	?

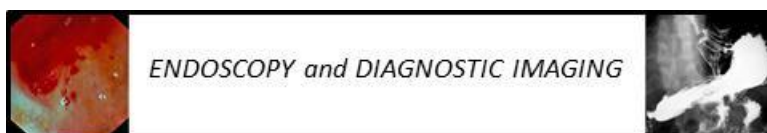
• Non-neoplastic gastric filling defects

➤ Bezoar

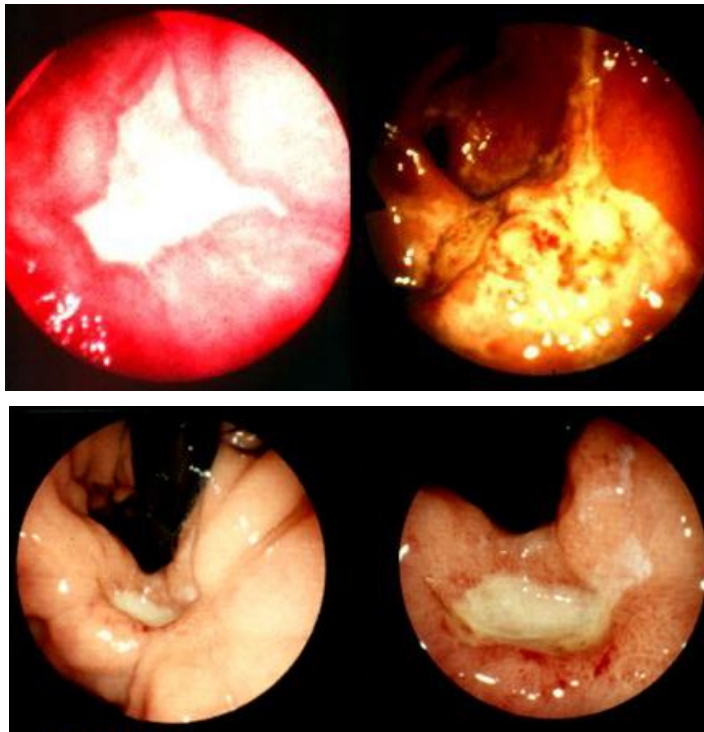
- Mottled, soft tissue mass (plain film)
- Filling defect
- Mottled, variegated appearance
- Not attached to gastric wall
- Moveable
- Barium collects in interstices of the concretion of ingested material

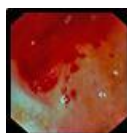
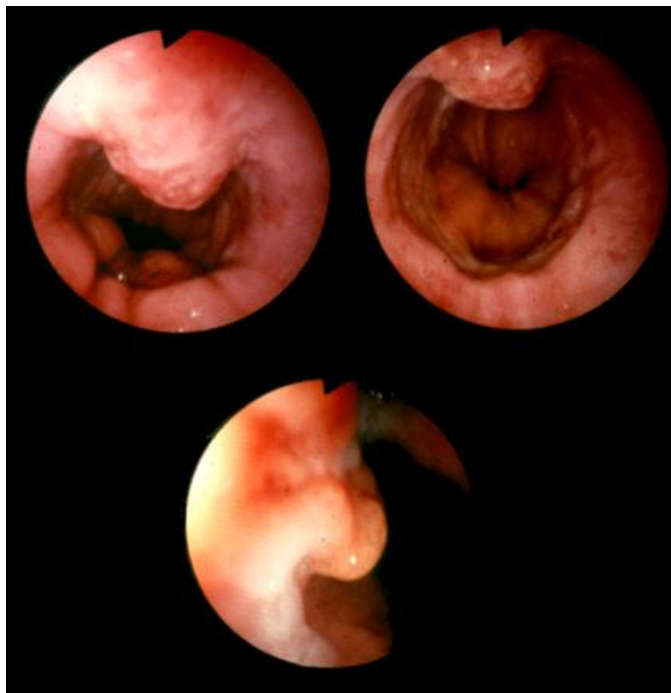
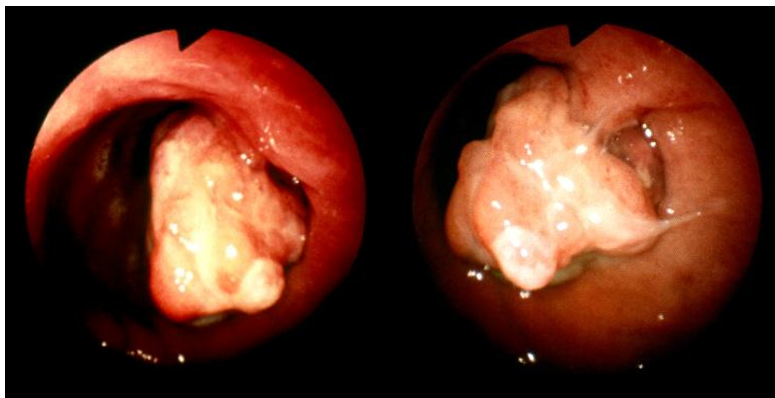
➤ Ectopic pancreatic rest

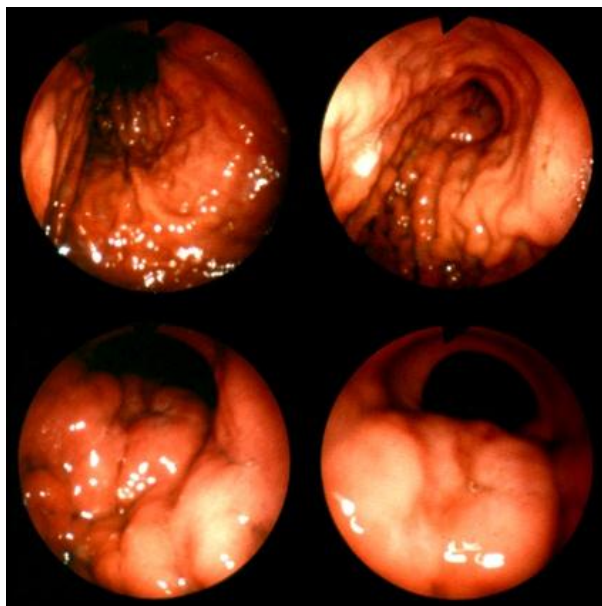
- Round filling defect submucosal
- Central umbilication (not an ulcer)
- Distal stomach

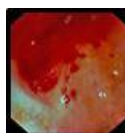
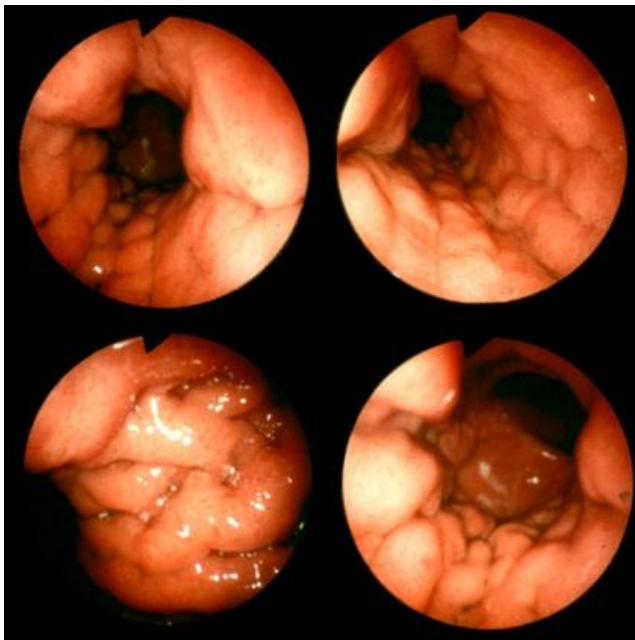
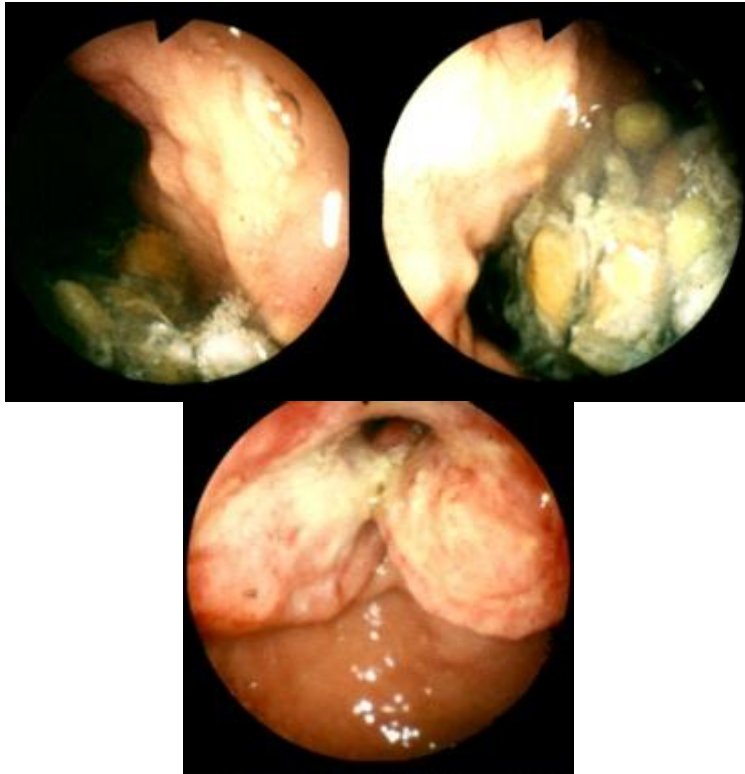


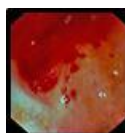
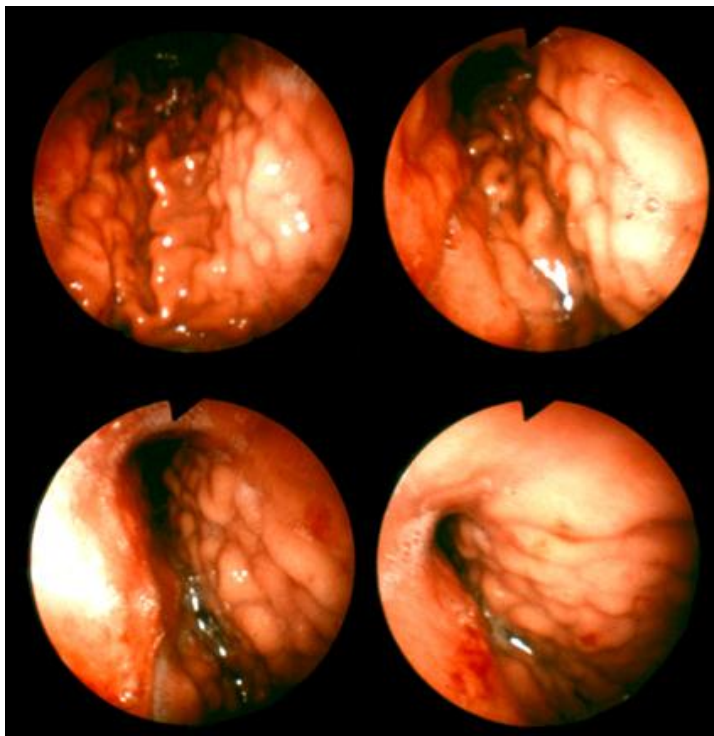
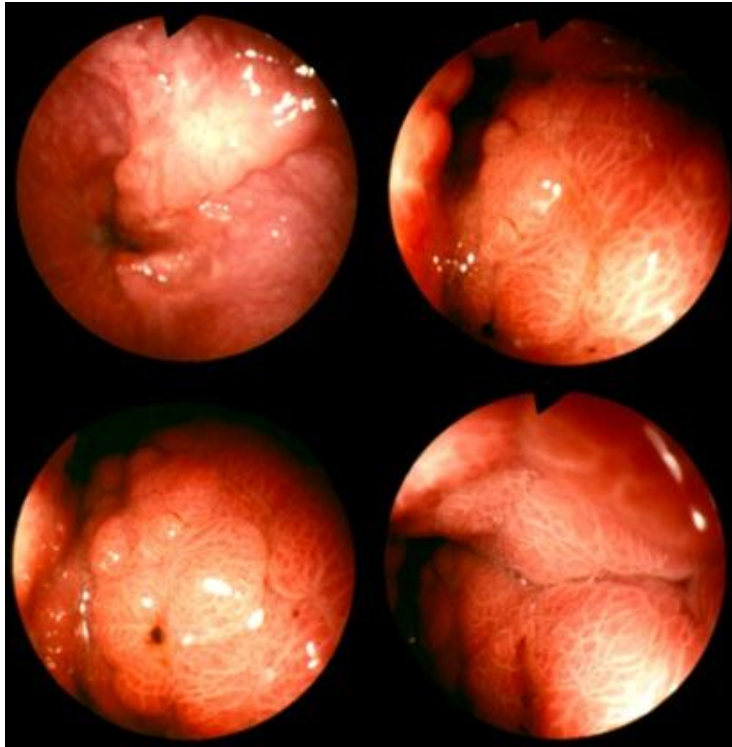
- Associated with concurrent pancreatic disease
 - Pancreatitis
 - Pseudocysts
 - Adenoma
 - Carcinoma
- Pseudotumor
 - History of surgical fundoplication
- Gastric varices
 - Filling defects in fundus
 - Polypoid
 - Lobulated (bunch of grapes)
 - Serpentine
 - Multiple
- Gastric cancer



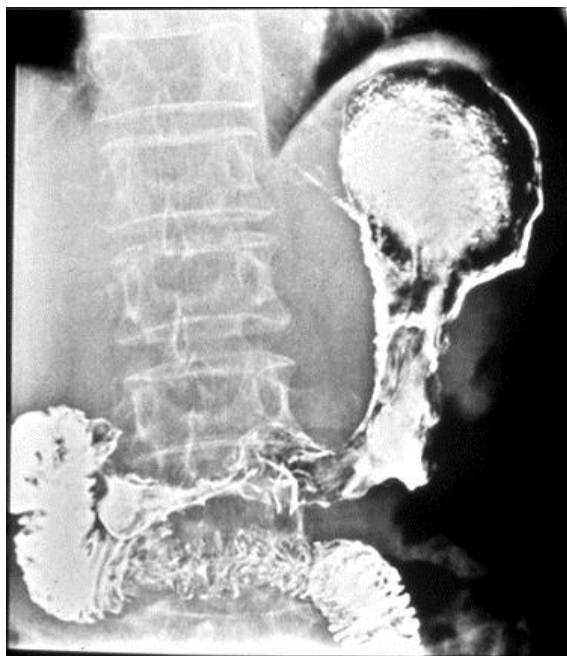
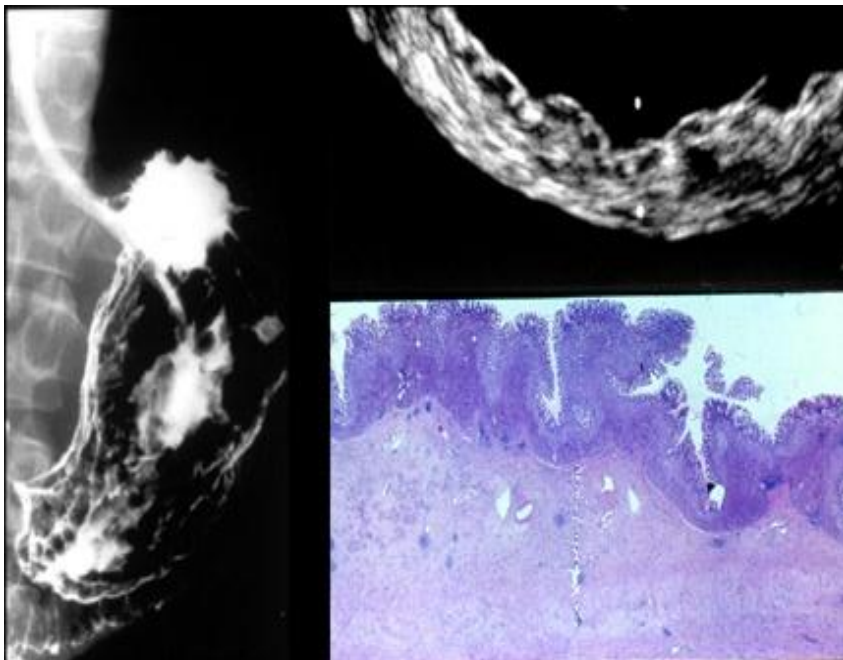


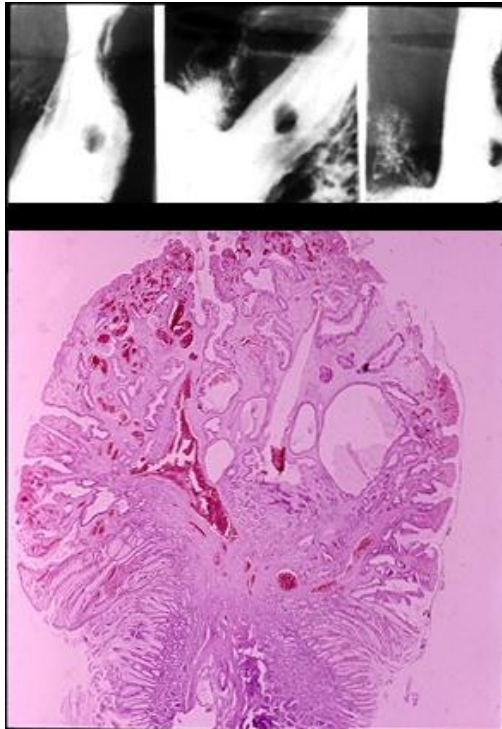






➤ Diagnostic imaging of gastric cancer

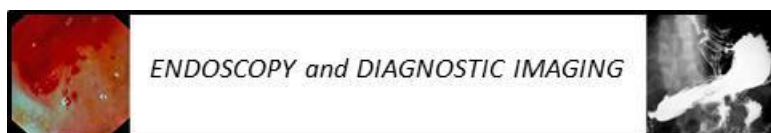




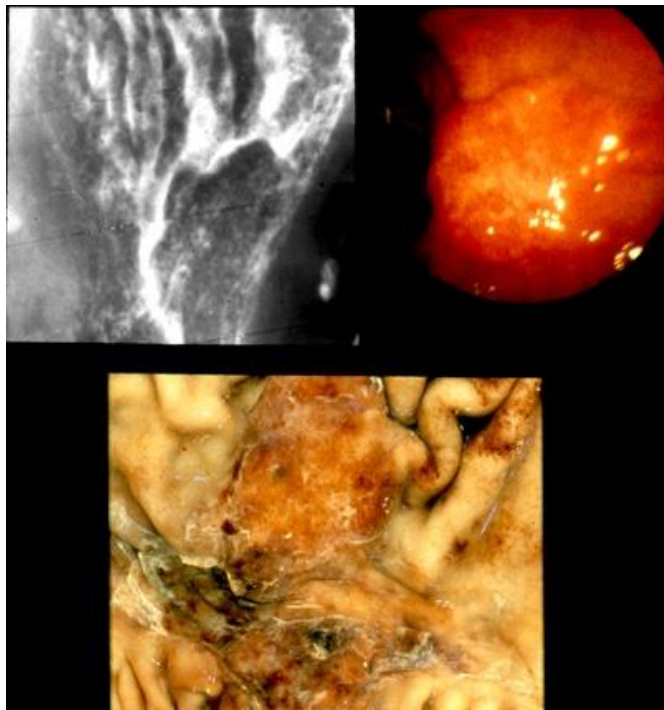
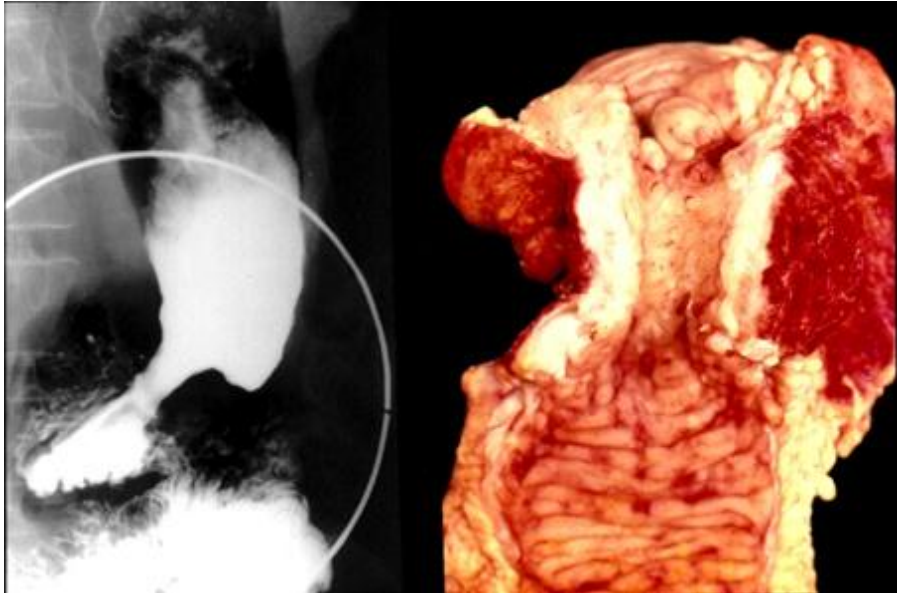
Gastric Stump Cancer

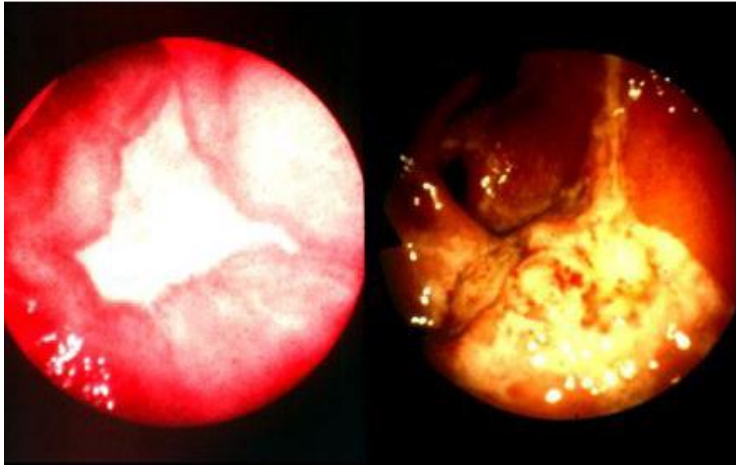
Overall incidence of cancer in the gastric remnant, 3.6–15.1%

- Amsterdam survey
 - Death due to stump cancer in 960 old gastrectomy patients >3.2%
 - Cancer rate detected by prospective endoscopic screening of 535 asymptomatic gastrectomy patient (>15 years) 4.1%
- Common sites for metastasis of gastric cancer
 - Liver
 - Lung
 - Supraclavicular lymph nodes
 - Abdominal lymph nodes
 - Peritoneum
 - Bone
- Unusual presentations of gastric cancer
 - Achalasia
 - Silent jaundice
 - Skin metastases
 - Intestinal obstruction
 - Fistula and perforation

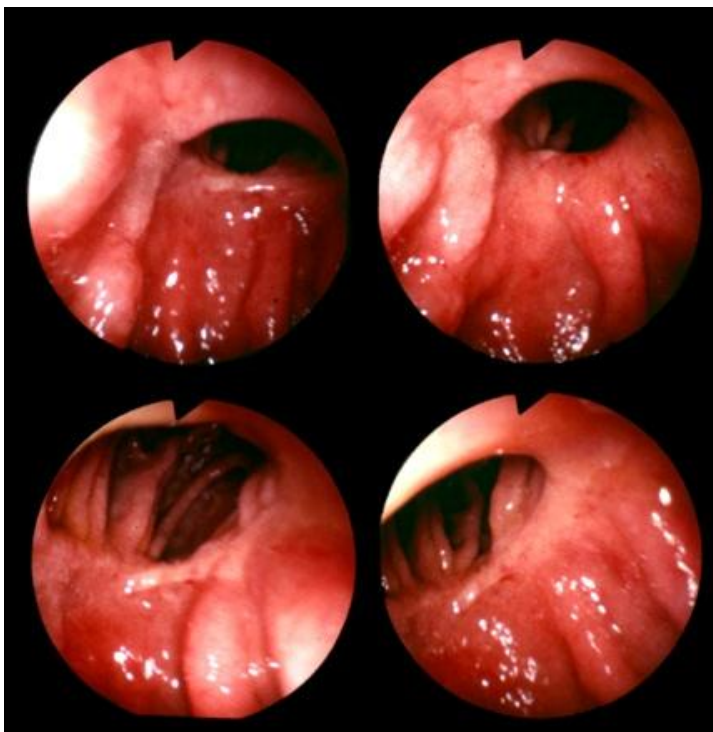


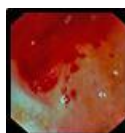
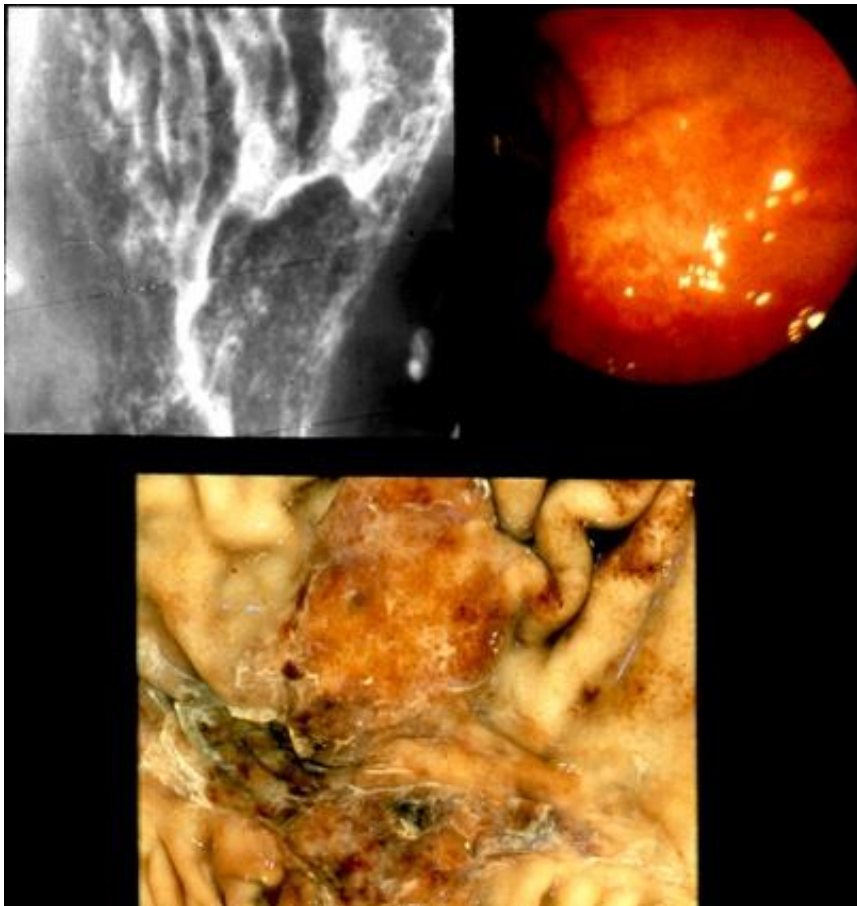
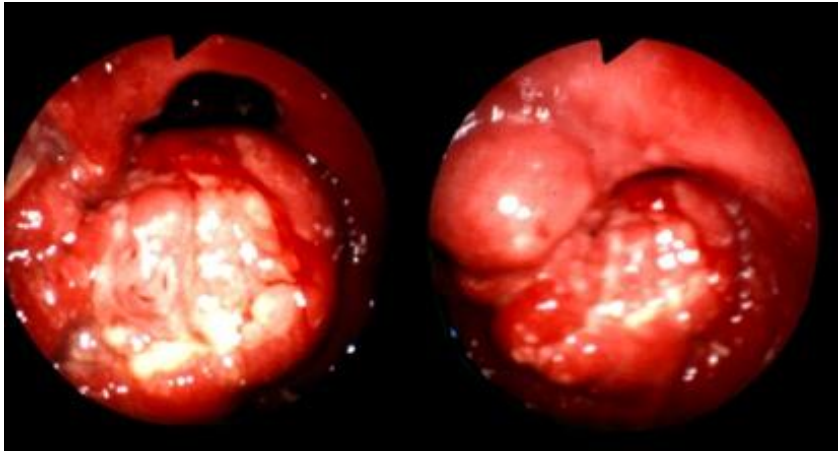
- Duodenal spread
 - Early gastric cancer
- Diagnostic imaging of gastric stump cancer





➤ Gastric Stump Cancer





Practice Pointers: Classification of Digestive Neuroendocrine Tumors

- Well-differentiated tumors
 - Carcinoid tumors of the gastrointestinal tract
 - Endocrine pancreatic tumors
- Poorly differentiated neuroendocrine carcinomas (based on):
 - Tumor localization
 - Tumor size
 - Angioinvasion
 - Hormone production
 - Histological grade
 - Proliferative index

Stomach: Clinicopathologic Classification of Neuroendocrine Tumors

- Well-differentiated tumor (carcinoid)

Benign behaviour: non-functioning, confined to mucosa submucosa, non-angioinvasive, ≤ 1 cm in size,

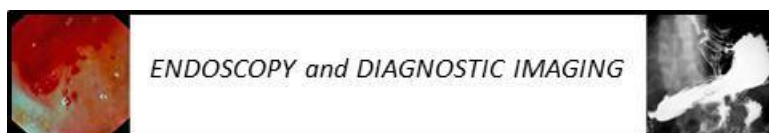
 - ECL cell tumours of corpus-fundus associated with hypergastrinemia, chronic atrophic gastritis (CAG, often with pernicious anemia) or MEN-1 syndrome
 - Serotonin-producing tumor
 - Gastrin-producing tumor
 - Uncertain behaviour: confined to mucosa-submucosa, >1 cm in size or angioinvasive
 - ECL cell tumors with/without CAG or MEN1 syndrome or sporadic gastrin, somatostatin or serotonin-producing tumors (rare)
- Well-differentiated endocrine carcinoma (malignant carcinoid)

Low-grade malignant: extending beyond submucosa, angioinvasive or metastasis

 - Non-functioning
 - ECL cell carcinoma, usually sporadic, rarely in CAG or MEN-1 syndrome
 - Gastrin, somatostatin or serotonin-producing tumors (rare)
 - Functioning
 - Gastrinoma
 - Serotonin-producing carcinoma with carcinoid syndrome
 - ECL cell carcinoma with atypical carcinoid syndrome
 - ACTH-producing carcinoma with Cushing syndrome
- Poorly differentiated endocrine carcinoma

High grade malignant (small to intermediate cell) carcinoma

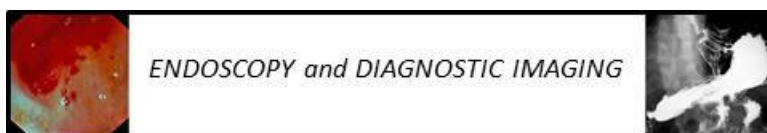
 - Usually non-functioning, occasionally with Cushing syndrome



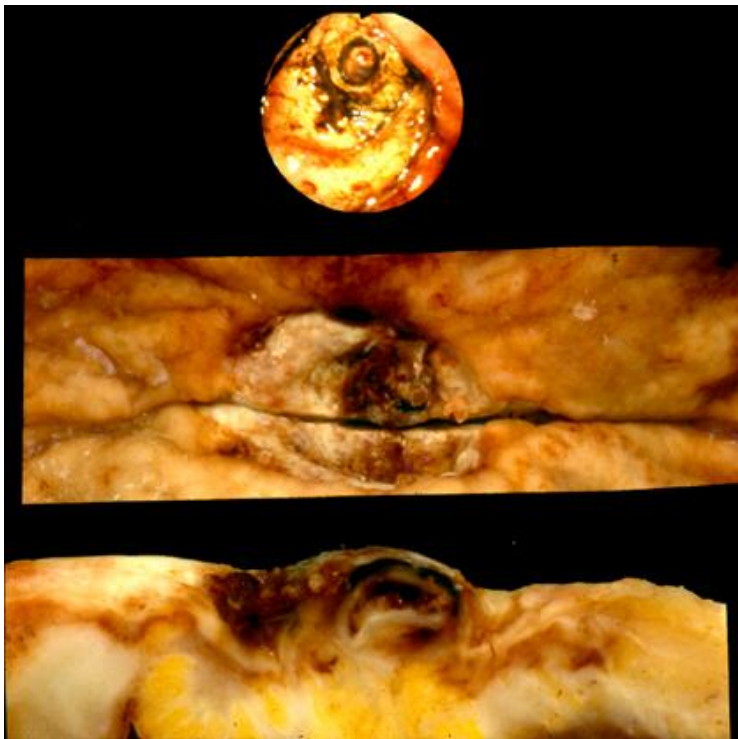
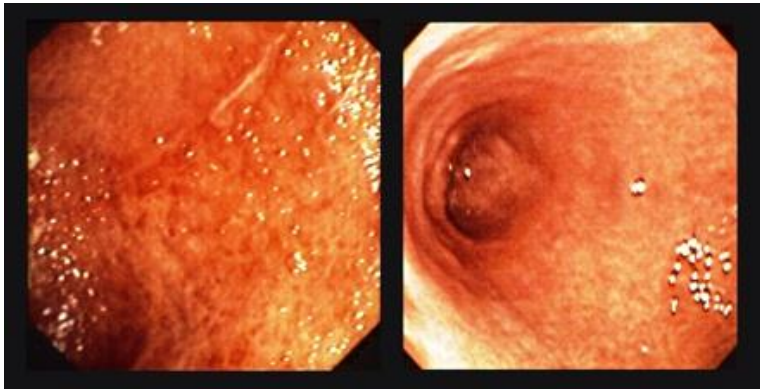
- The pharmacodynamic action of synthetic somatostatin and octreotide in the human GI tract
 - Inhibition of neuroendocrine secretion
 - Gut peptides
 - Pancreatic peptides
 - Inhibition of exocrine secretion
 - Salivary gland (amylase)
 - Stomach (acid, pepsin, intrinsic factor)
 - Pancreas (enzymes, bicarbonate)
 - Liver (bile flow)
 - Inhibition of intestinal transport
 - Absorption of glucose, fat, amino acids
 - Inhibition of motility
 - Stimulated intestinal secretion
 - Stomach (late phase of gastric emptying)
 - Gallbladder contraction
 - Small intestinal transit time
 - Early gastric emptying
 - Migrating motor complex
 - Stimulation of motility
 - Wedged hepatic venous pressure
 - Portal pressure
 - Inhibition of splanchnic hemodynamics
 - Splanchnic blood flow

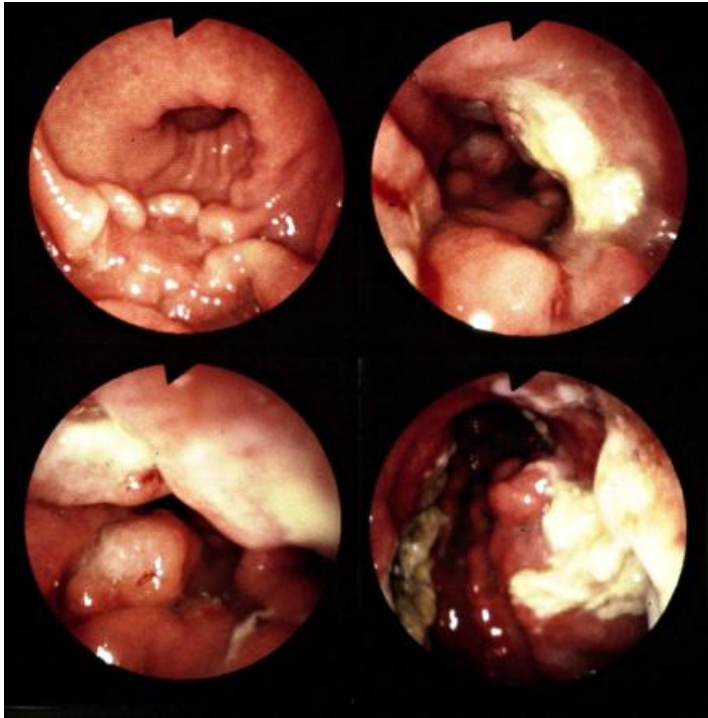
GASTRIC LYMPHOMA

- Gastric Malt Lymphoma / Maltoma: Essential Features
 - Lymphoepithelial lesions
 - Centrocytic-like cell (low-high grade)
- Endoscopic differential diagnosis of primary gastric lymphoma
 - Secondary gastric localization other lymphomas (nodal NHL, mantlecell-lymphoma)
 - Gastritis / peptic ulcer
 - Gastric carcinoma
 - Menetrier's disease
 - Syphilis
 - Gastric metastases (lobular-type breast cancer)



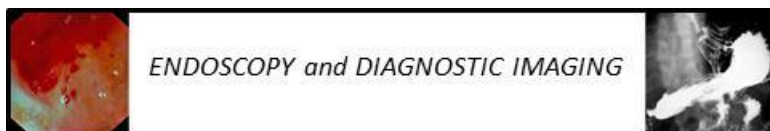
➤ Gastric lymphoma





Diagnostic imaging

- Miscellaneous gastric conditions
 - Thickened folds
 - Cardia/ fundus
 - Varices
 - Ménétrier disease
 - Antrum
 - H.pylori gastritis
 - Anywhere
 - Crohn's disease
 - Zollinger – Ellison syndrome (ZES)
 - Lymphoma
 - Miscellaneous (et al.)
 - Cardia / fundus
 - Diverticulum
 - Pseudotumor
 - Rest of stomach
 - Emphysematous gastritis
 - Partial diverticulum
 - Volvulus



- Barium Rests
- Erosions
- Peptic ulcer
- Carcinoma

➤ Narrowed stomach (linitus plastica)

Differential: intramural diverticulum may look like sump ulcer, but no surrounding mass effect, and changes shape with peristalsis

➤ Crohn's disease

- Thickened folds
- Multiple small erosions with halo (apthous ulcers)
- Ulcers, confluent serpiginous
- Mucosa cobblestone
- Fibrosis
- Strictures
- Distal half of stomach
- Often with associated duodenal ulcer

➤ Varices

- GE junction
- May be associated with esophageal varices

➤ Diverticulum

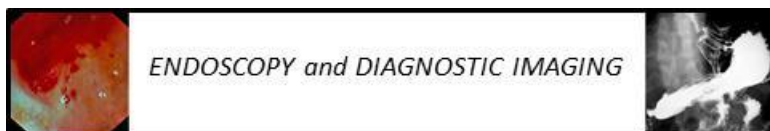
- Pouch filled with barium
- Posterior surface of fundus near the GE junction
- Mucosal folds in pouch
- May change size and shape

➤ Partial gastric diverticulum

- Definition: "protrusion of [gastric] mucosa into the muscular wall of the stomach without disturbing the serosa"
- Intramural collection of barium
- Greater curve
- Narrow neck
- Barium – filled pouch changes size/ shape
- May be associated with ectopic pancreatic tissue

➤ Emphysematous gastritis

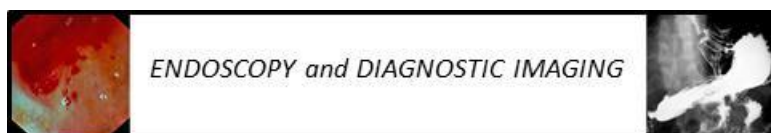
- Intramural gastric air
- Cause
 - Infection
 - E.coli
 - Clostridium perfringens
 - Ischemia
 - Ingestion of corrosive

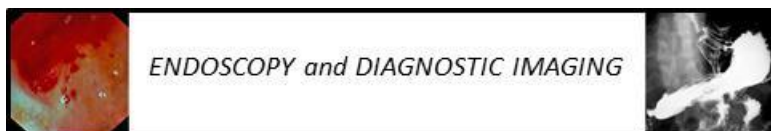


- Obstruction of stomach

Gastric volvulus

- Organo axial
 - 180° torsion along longitudinal axis
 - Greater curvature is superior to lesser curve
 - Gastric body is superior to fundus (“upside – down” stomach)
- Mesenteroaxial
 - 180° torsion about the gastric mesentery
 - Pylorus and antrum folded anteriorly and superiorly



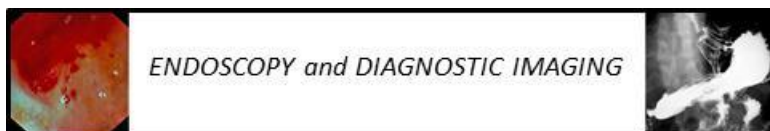


STOMACH DIAGNOSTIC IMAGING

CLINICAL SKILLS

Self-assessment

**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**

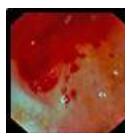


Case 1

38 year old female presents in ER with abdominal pain and distention one week after discharge for vagotomy and pyloroplasty for intractable dyspepsia.

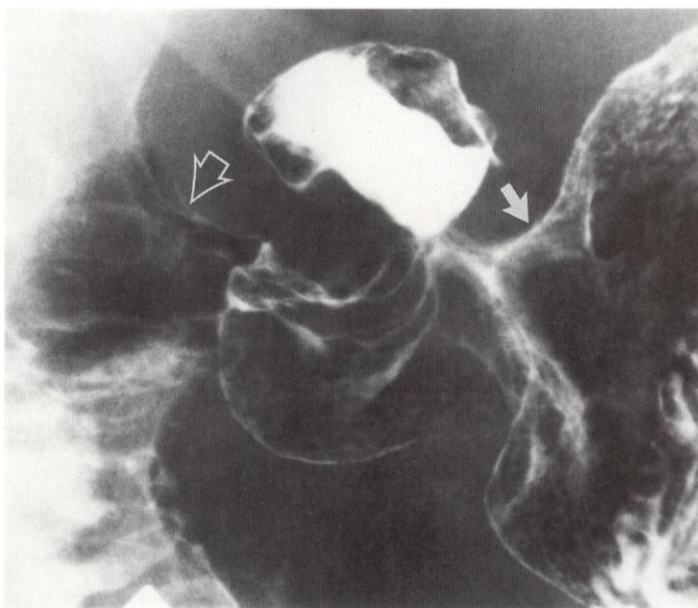
Case 2

72 year old male presents with weight loss and early satiety.



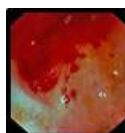
Case 3

75 year old woman with osteoarthritis presents with dyspepsia.

**Case 4**

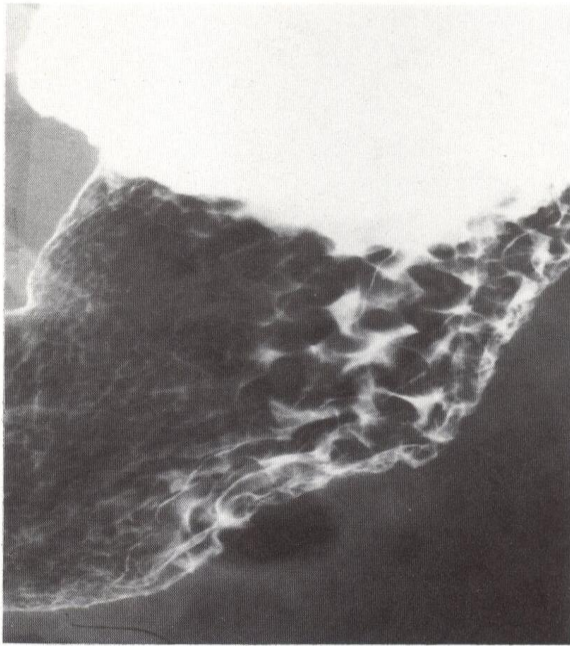
68 year old man with almost life-long history of dyspepsia

D

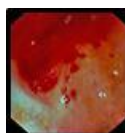
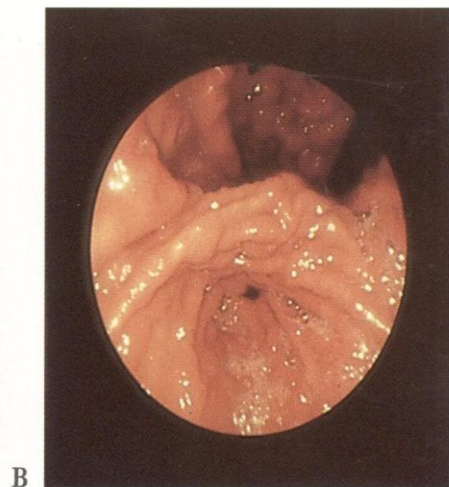
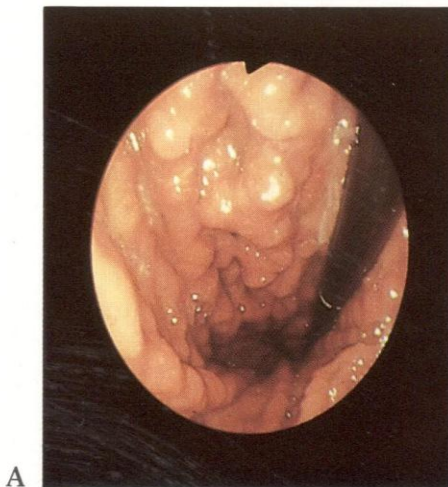


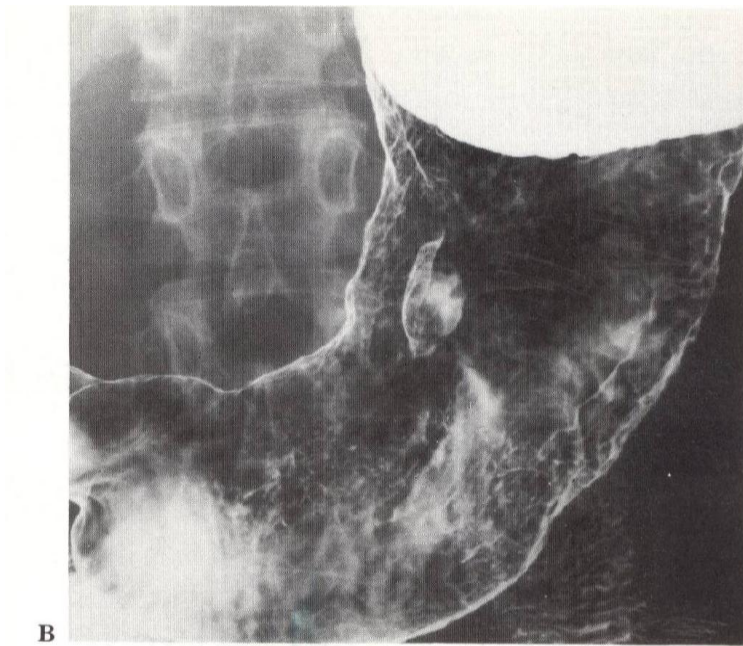
ENDOSCOPY and DIAGNOSTIC IMAGING



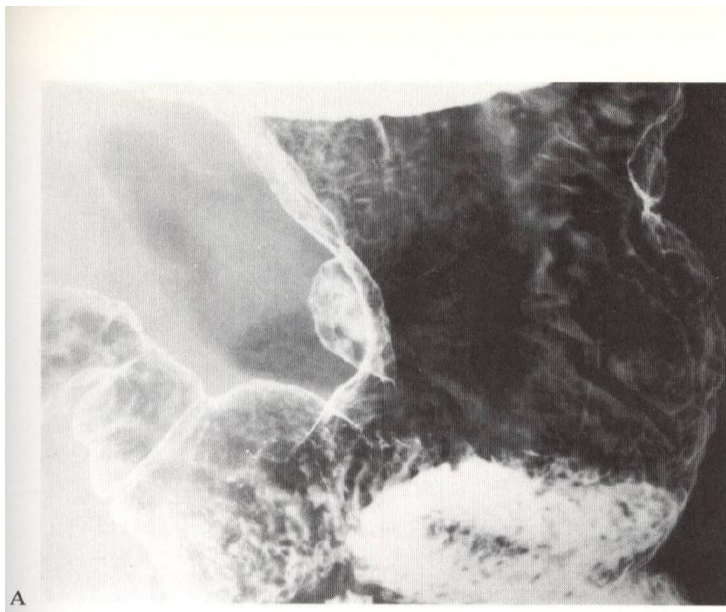
Case 5

60 year old woman
with history of vague
dyspepsia, mild
microcytic anemia dn
hypoalbuminemia

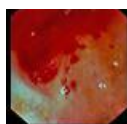


Case 6

70 year old woman with 10 year history of osteoarthritis, on an NSAID for 6 months

Case 7

Same patient and barium study as above



ENDOSCOPY and DIAGNOSTIC IMAGING

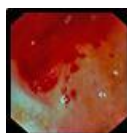


Case 8

35 year old man with 5 year history of dyspepsia, not on ASA/ NSAIDs; urea breath test positive

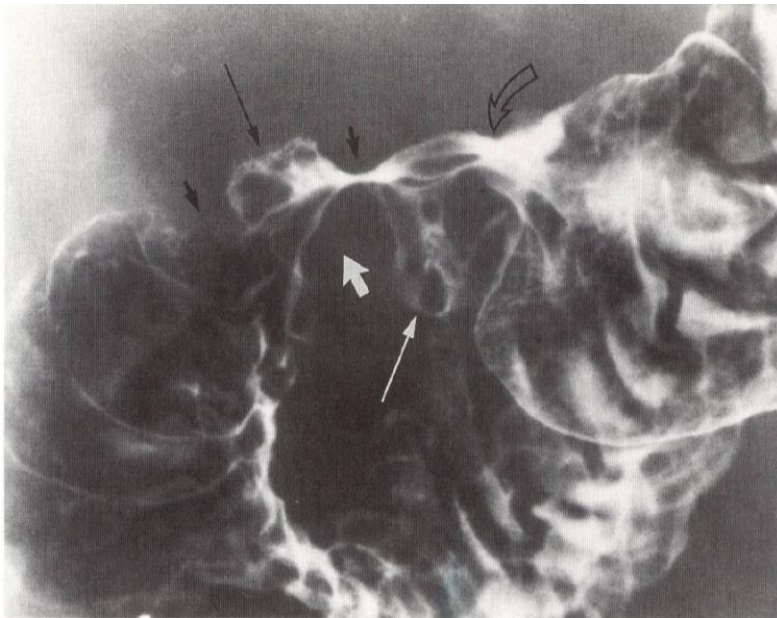
Case 9

Same patient and barium study as above

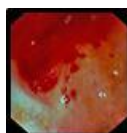


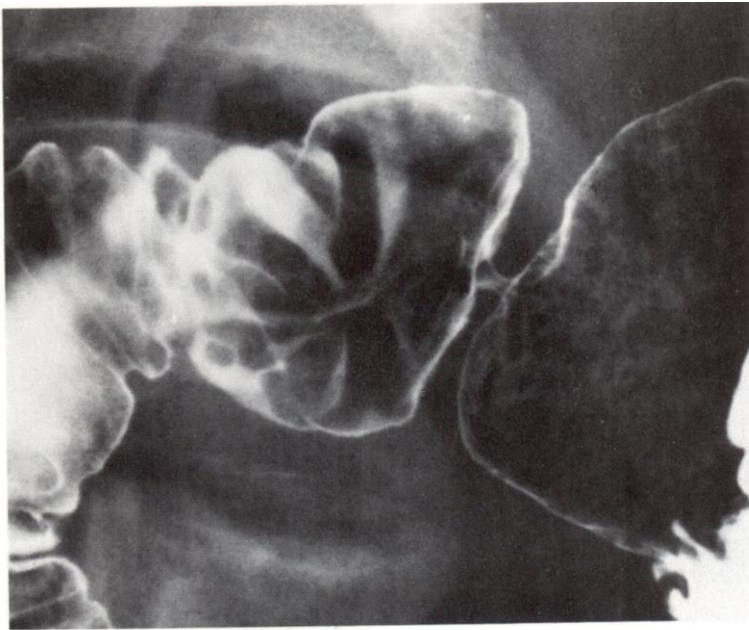
Case 10

Upper GI series performed in 55 year old woman while awaiting gastroscopy

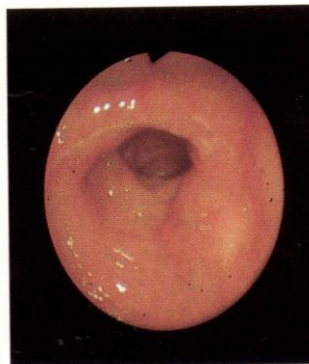
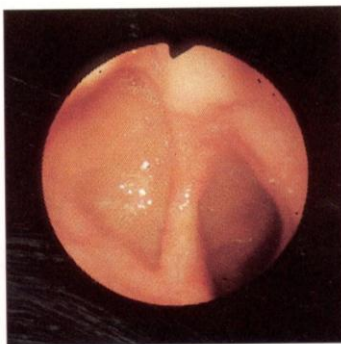
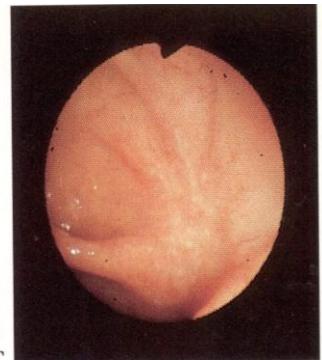
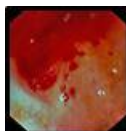
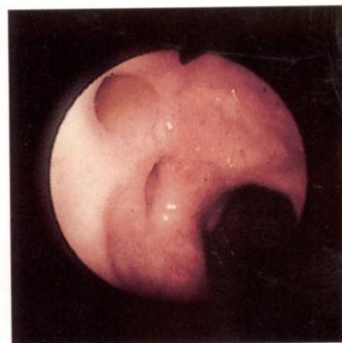
Case 11

The "Arrow Sign" patient with chronic dyspepsia



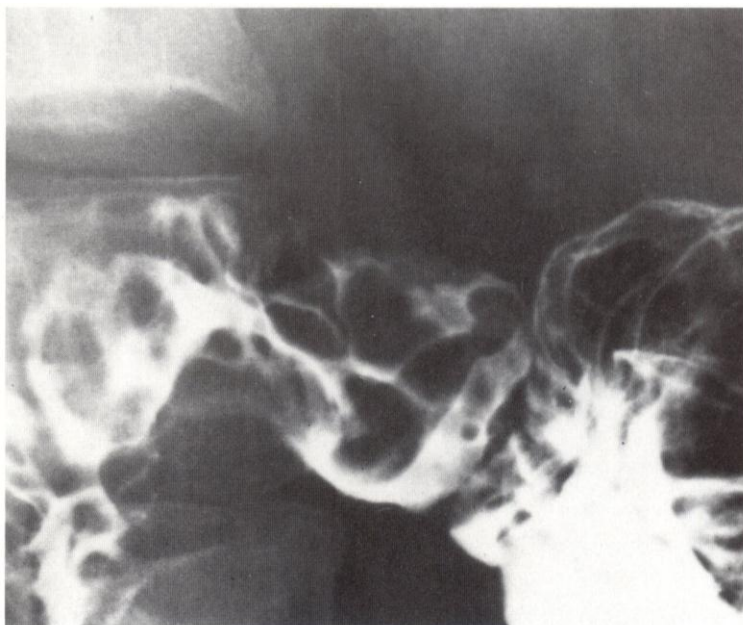
Case 12

Previous upper GI bleed, *H. pylori* positive, treated with triple therapy but dyspepsia persists

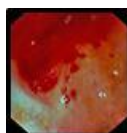
**B****C****E**

Case 13

Dyspeptic 51 year old man, worried about having gastric cancer

Case 14

Nausea, indigestion, but no bleeding or weight loss in 60 year old woman



Stomach (upper GI series)

1. Gastric dilation
2. linitis plastica
3. Penetrating giant gastric ulcer from greater curve to transverse colon
4. Prepyloric ulcer: Large Prepyloric Ulcer Indenting Antrum (Closed Arrow) and duodenum (Open Arrow) by a surrounding inflammatory mass.
5. Prominent gastric folds.
6. Gastric ulcer: Posterior wall ulcer in profile.
7. Gastric ulcer: Posterior wall ulcer en face.
8. Deformed duodenal bulb: Radiating folds, barium niche (closed arrow), surrounding edema (open arrows).
9. Duodenal narrowing, spasm.
10. Inferior "DU" in distal bulb.
11. Duodenal ulcer (DU): Deformed duodenal bulb, narrow pylorus (open curved arrow), pseudodiverticulum (long white arrow), ulcer crater (long black arrow), edema on both sides of ulcer (short black arrows), and incisura opposite ulcer (short white arrow).
12. Healed DU.
13. Duodenal filling defects: Multiple small polygonal defects in duodenal cap from ectopic gastric mucosa.
14. Duodenal filling defects: Multiple larger rounded filling defects in duodenal cap, from nodular hyperplasia, Brunner's gland hyperplasia, or duodenitis.

Please compare your findings with those described in the previous material.



STOMACH

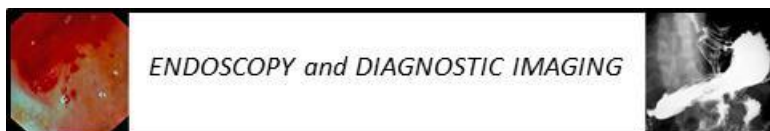
ENDOSCOPIC IMAGING

CLINICAL SKILLS

Self-assessment

**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**

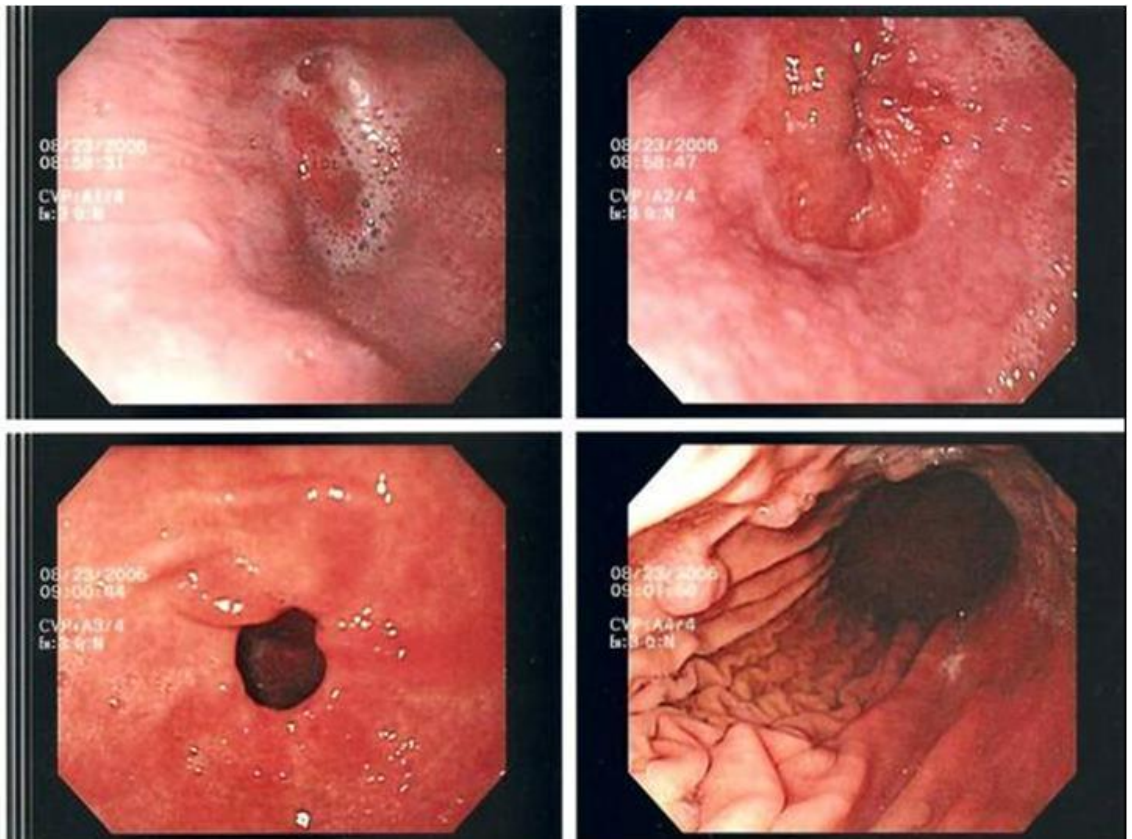
*Provided through the courtesy of Dr. Edgar Jaramillo, Center of
Gastrointestinal Disease, Ersta Hospital, Stockholm, Sweden, and
through the courtesy of Dr. C. Noel Williams, Dalhousie University and
University of Alberta.*



Describe the following gastric endoscopy photographs, give the differential diagnosis, and state the most likely endoscopic diagnosis.

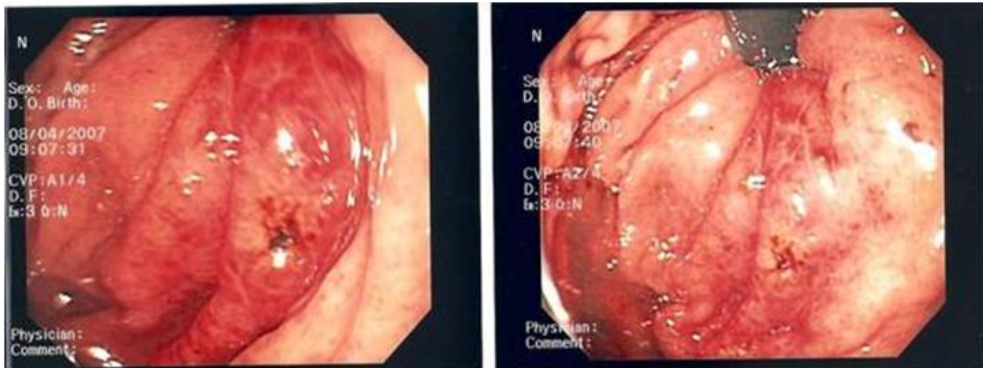
Case 1

A 54 year old obese woman with “gas” and bloating following a fundoplication. Please describe the endoscopic findings, give the most likely causes, and provide your management.



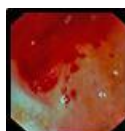
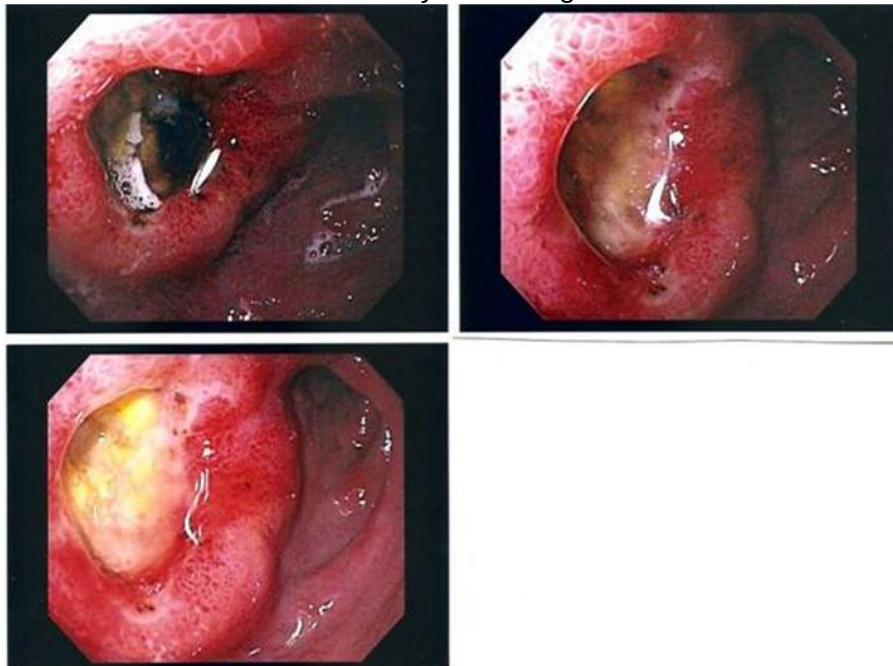
Case 2

A 48 year old man with a B cell lymphoma involving the tail of the pancreas presents with an upper GI bleed. Please describe the endoscopic findings, give the differential diagnosis, speculate on the mechanism and outline the management.



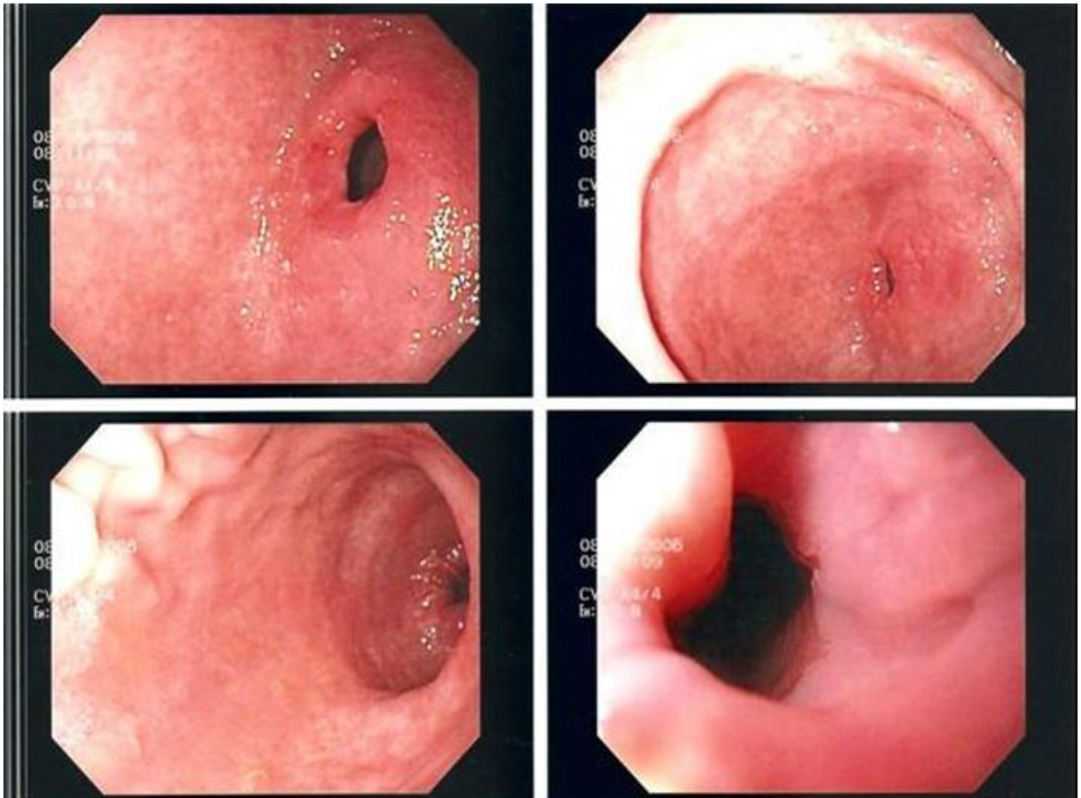
Case 3

A 62 year old man presents with epigastric pain. There was no use of ASA/NSAID/Coxibs/bisphosphonates; normal gastrin. Please describe the gastric endoscopic findings and speculate on the causes and mechanisms of each and outline your management.



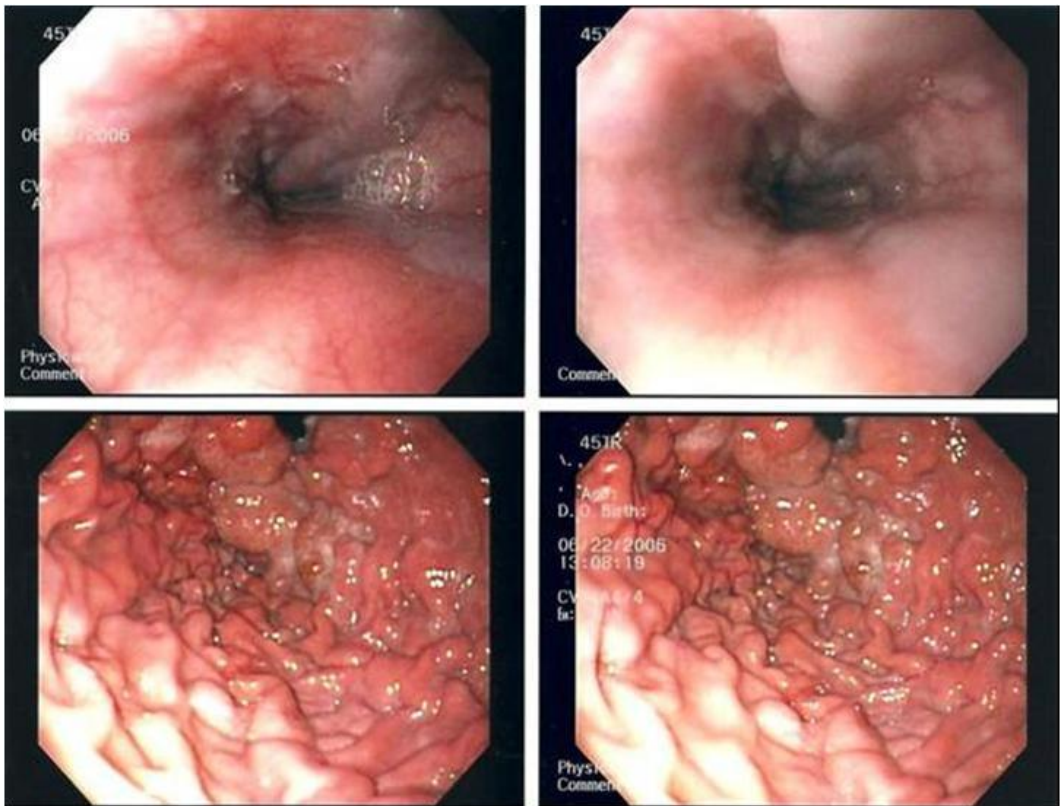
Case 4

A 70 year old woman is treated for 12 weeks with a PPI for a benign pre-pyloric ulcer. She is now asymptomatic. Endoscopy is repeated. Please describe the endoscopic findings, and your management.



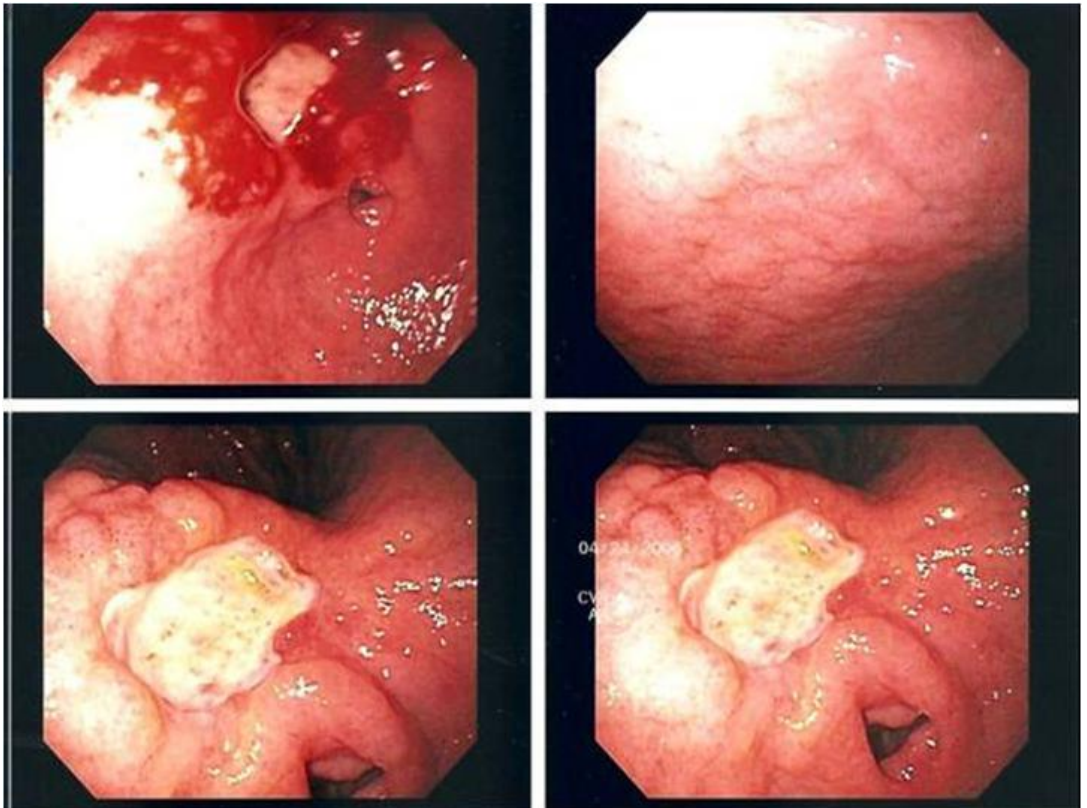
Case 5

A 29 year old man presents with an upper GI bleed, jaundice, and sudden onset of severe epigastric pain radiating to the back. There are no extrahepatic signs of chronic liver disease. Please describe the endoscopic findings, give a differential diagnosis of the causes, and give your management.



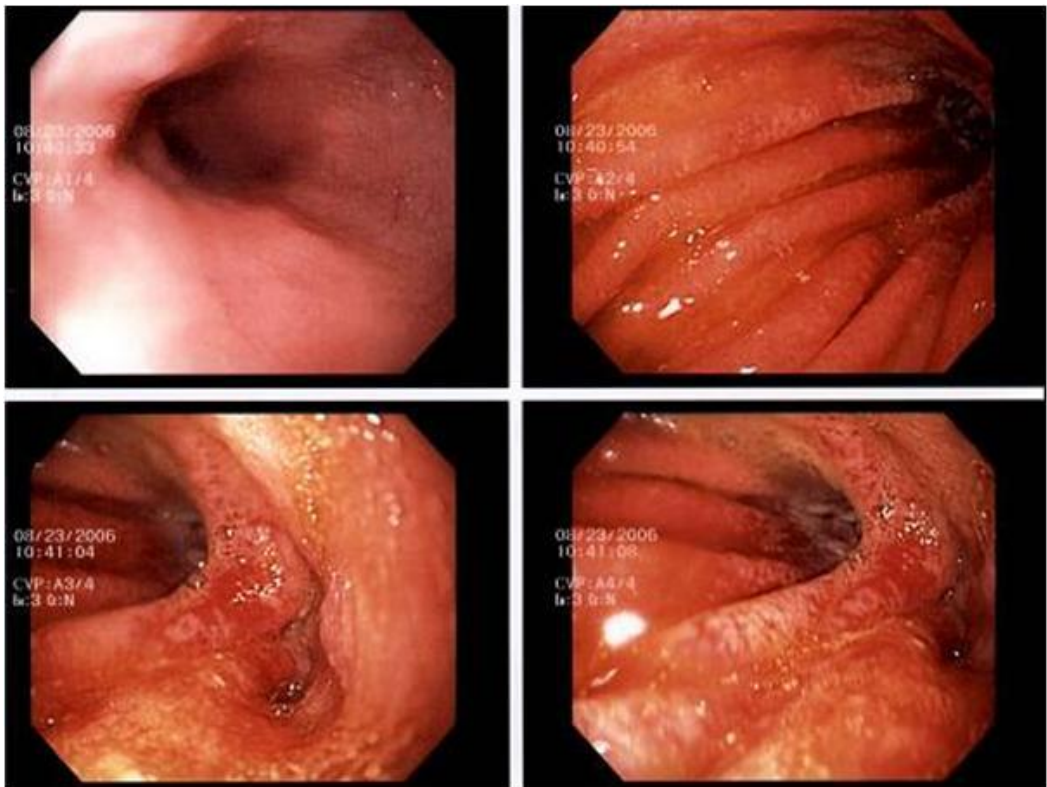
Case 6

A 79 year old woman presents with recent onset epigastric pain following 4 weeks of medical treatment for a gastric ulcer. Please describe the endoscopic findings, and outline your management.



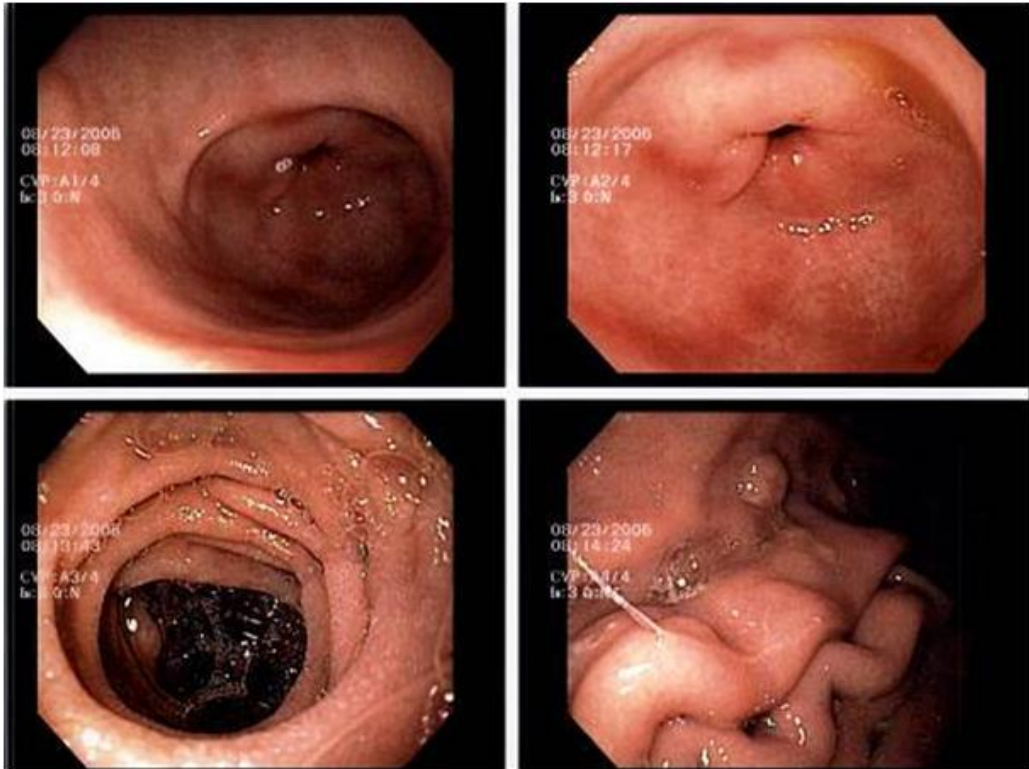
Case 7

A 66 year old woman presented with dyspepsia. A mass lesion in the stomach (carcinoid) was treated with a hemigastrectomy (Billroth II). She presents 8 years later with iron deficiency anemia. The fasting serum gastrin concentration was markedly increased. Please describe the findings and management.



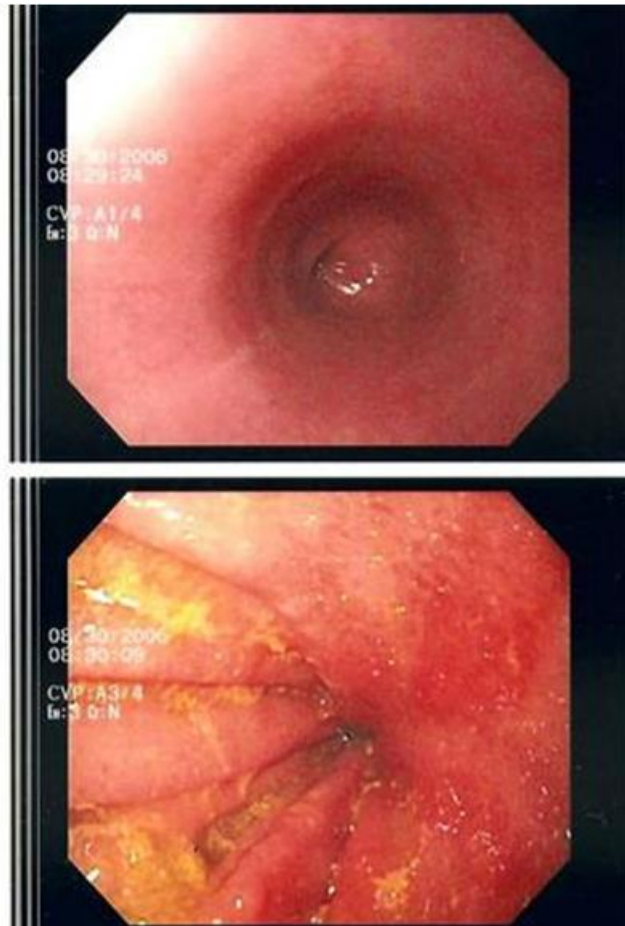
Case 8

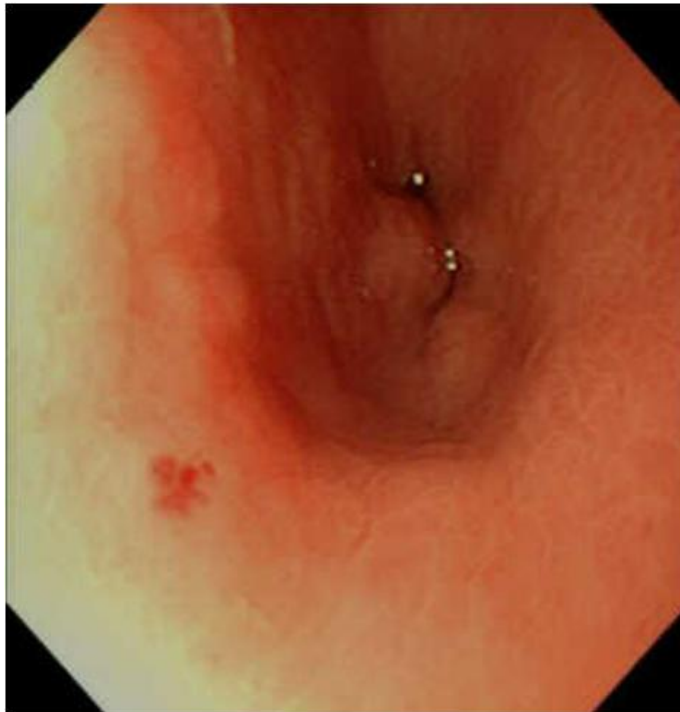
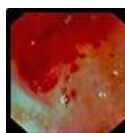
A 64 year old woman with a long history of recurrent, severe dyspepsia, presented with dyspepsia and diarrhea while on a PPI. Her fasting gastrin concentration was 750 pg/ml. Please describe your endoscopic findings and management.

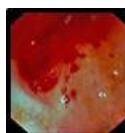
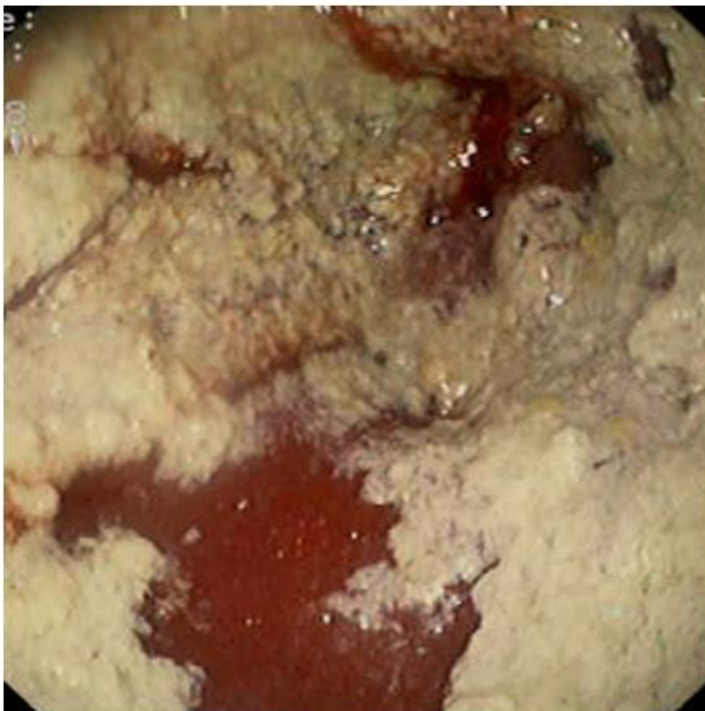


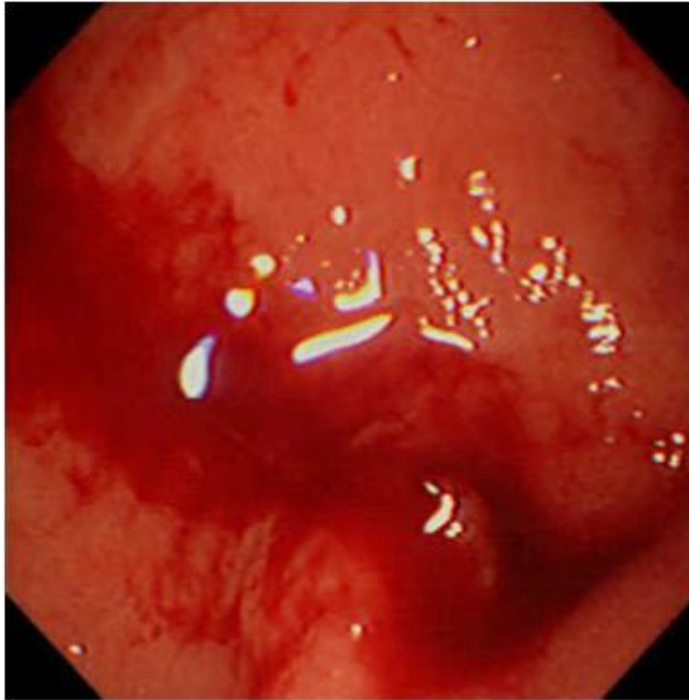
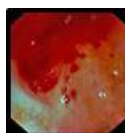
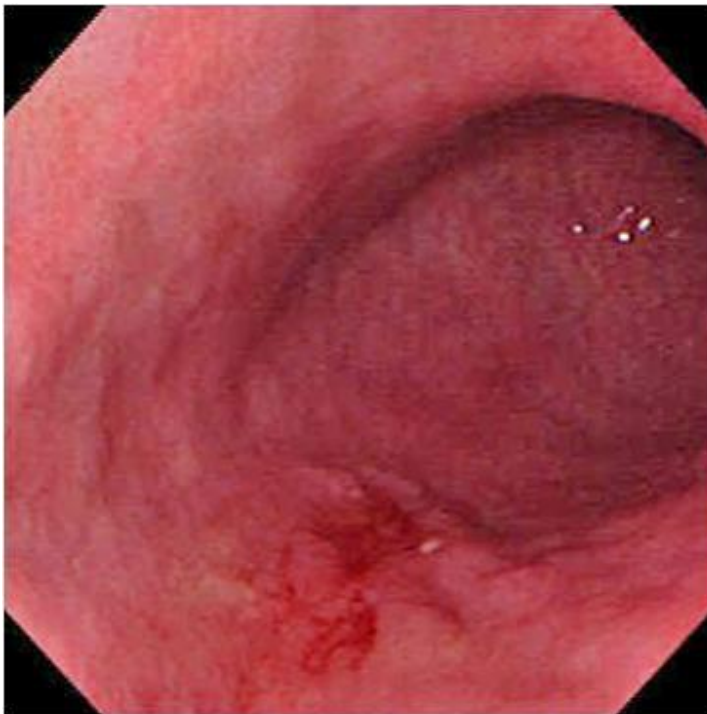
Case 9

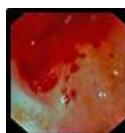
A 63 year old woman with a previously drained choledochal cyst with hepatojejunostomy; A Billroth I procedure was performed 20 years ago for resistant PUD. She now presents with dyspepsia. Please give the endoscopic findings and the differential diagnosis.

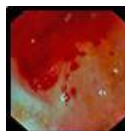
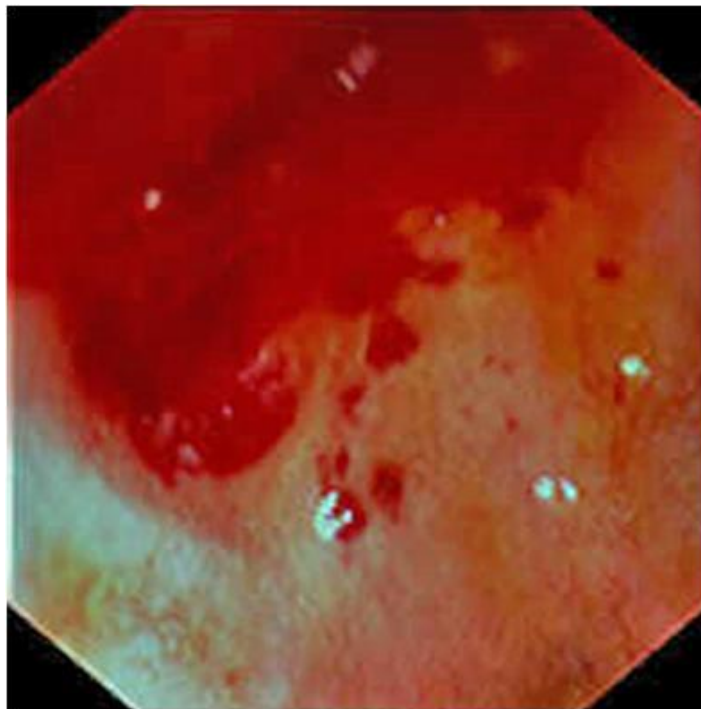


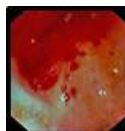
Case 10**Case 11**

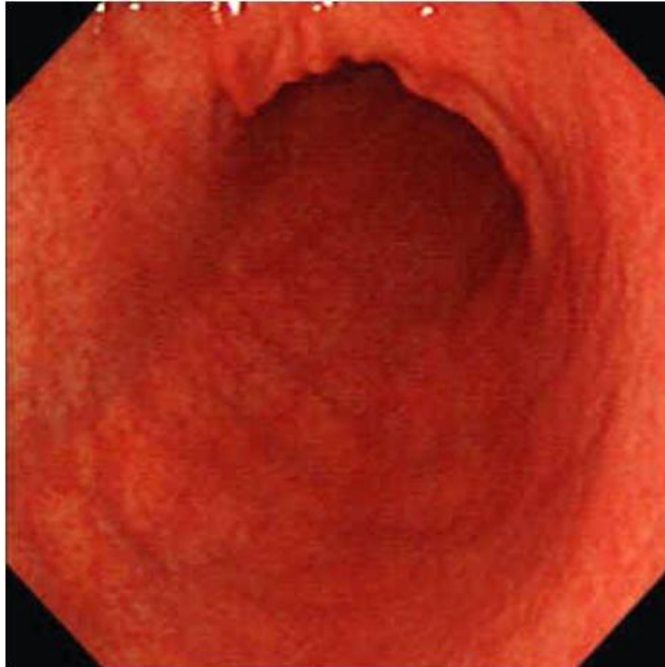
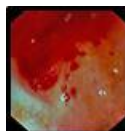
Case 12**Case 13**

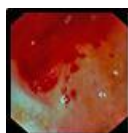
Case 14**Case 15**

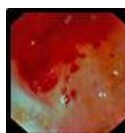
Case 16**Case 17**

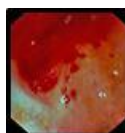
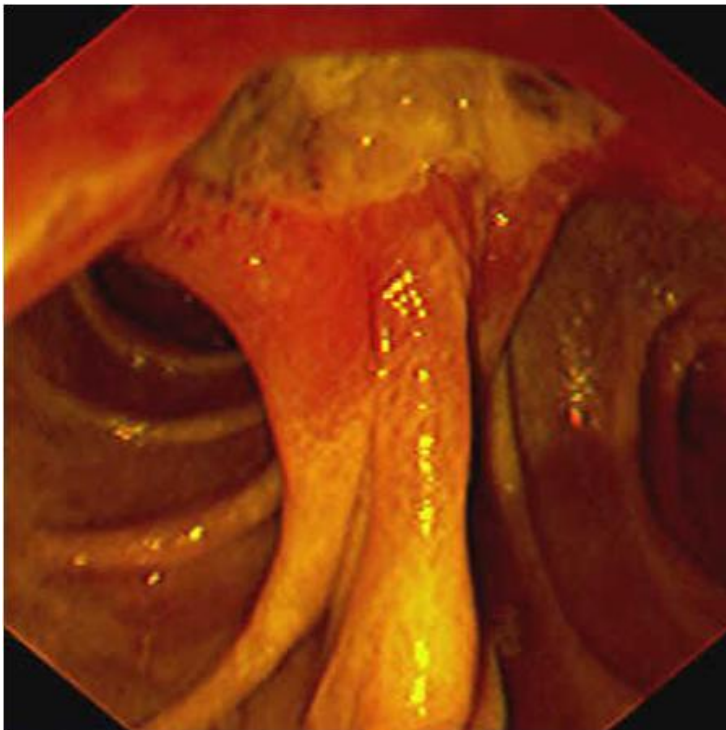
Case 18**Case 19**

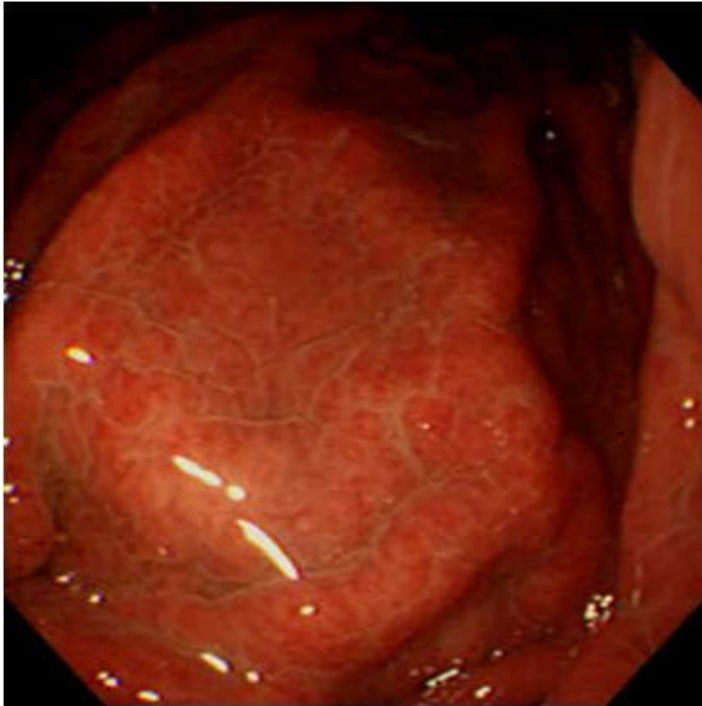
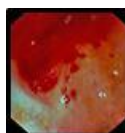
Case 20**Case 21**

Case 22**Case 23**

Case 24**Case 25**

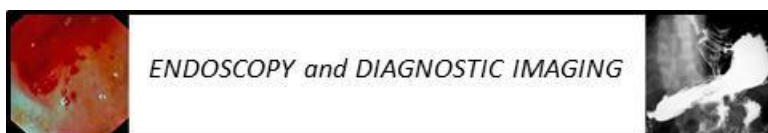
Case 26**Case 27**

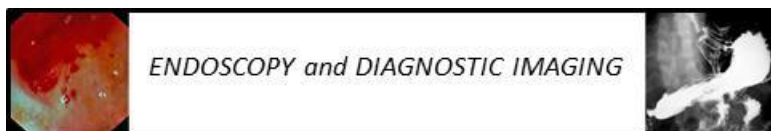
Case 28**Case 29**

Case 30**Case 31**

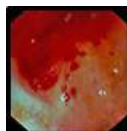
Part B. case answers

1. Fundic gastric polyps
2. Gastric cardia varices: splenic vein thrombosis
3. Ulcer, possibly H. pylori associated
4. Antral erosions, ?Hp, ?NSAIDs
5. Esophageal and gastric varices; gallstone pancreatitis, PV thrombosis
6. GU, possible gastric Ca
7. BII, stoma, GDR/GCa
8. Thick gastric folds, gastric polyp, possible MEN1
9. Bile gastritis
10. Angiodysplasias
11. Billroth I
12. Cancer in gastric remnant
13. Candidiasis
14. Dieulafoy's lesion
15. Early gastric cancer
16. Esophago-gastro-duodenoscopy
17. Esophago-jejunostomy
18. Fundic gland polyps in FAP
19. Upper GI bleed
20. Upper GI bleed, gastric ulcer
21. Upper GI bleed, gastric ulcer
22. Gastric atrophy
23. Gastric polyps
24. Intestinal metaplasia in stomach
25. Gastric lymphoma
26. Metastasis to stomach
27. NSAID gastropathy
28. Pyro bezoar
29. Stomal ulcer, Billroth II surgery
30. Portal hypertensive gastropathy
31. Watermelon stomach





SMALL INTESTINE

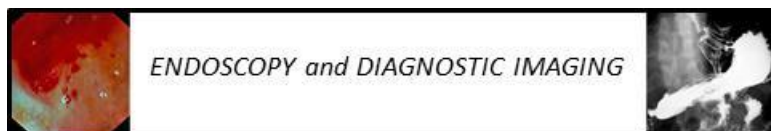


ENDOSCOPY and DIAGNOSTIC IMAGING



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Crohn disease	285
Diarrhea	291
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Endoscopic imaging	319



SMALL INTESTINE

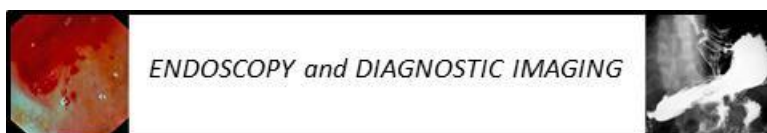
“Sharpening Knowledge to Enhance Clinical Skills”

Useful background: Questions and Answers

GI BARRIER

- Give the components of the GI mucosal barrier, and for each give their function to protect against enteric infection.

Components	Function
➤ LUMEN	
○ Gastric acid (pH)	- Breakdown of ingested antigens
○ Bile acids	- Breakdown of ingested antigens
○ Intestinal peristalsis	- Block penetration of ingested antigens
○ Indigenous microflora	Competitive inhibition
	- <i>Direct</i> : competition for essential nutrients and bacterial receptor sites; creation of restrictive physiological environments; secretion of antibiotic-like substances
	- <i>Indirect</i> : chemical modification of bile salts and dietary fats, induction of protective Ig responses, stimulation of peristalsis
➤ Epithelial membrane	
○ Epithelium: glycocalyx, villi	- Innate immune response
	- Antigen presentation
	- Block penetration of ingested antigens
○ Defensins	- Antimicrobial peptides
○ Trefoil factors	- Protection from a variety of deleterious agents (bacterial toxins, chemicals and drugs); provide restitution after mucosal injury
○ Mucus/mucins	- Block penetration of ingested antigens
○ Proteases: pepsins, pancreatic enzymes	- Breakdown of ingested antigens
○ Secretory-IgA (s-IgA)	- Binds bacteria and dietary antigens (thus limiting absorption/immune response)
	- Phagocytosis
	• Resistant to digestion



- Secreted
- Does not activate complement cascade
- Does not participate in antibody-dependant cytotoxicity.

➤ GALT

- GALT-associated IgA, IgG^a, IgM^a (serum)
 - Clear antigens penetrating gastrointestinal barrier/systemic immunity
 - Assist in opsonization and phagocytosis of antigens^a
- Lymphoid follicles in lamina propria (LP)
 - Clear antigens penetrating gastrointestinal barrier

Components	Function
○ Intraepithelial lymphocytes (IEL)	- Innate and acquired immune responses
○ Mesenteric lymph nodes	- Phagocytosis and antigen presentation

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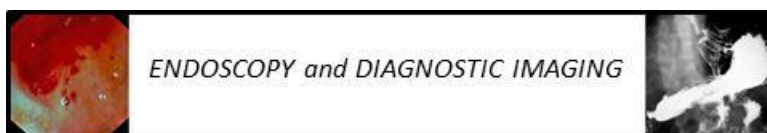
CELIAC DISEASE

➤ Definition

- Children
 - Presence of morphological changes in jejunal mucosa
 - Morphological improvement upon gluten withdrawal
 - Exacerbation after reintroduction of gluten
- Adults
 - Presence of morphological changes in jejunal mucosa
 - Unequivocal clinical and biochemical response to gluten withdrawal
 - (Morphological improvement)

➤ Immunological Disorders

- Increase IgA and IgM plasma cells in lamina proptia
- Marked epithelial lymphocytic permeation
- Increased serum IgA and decreased serum IgM levels
- Presence of IgM anti gliadin, IgG anti-reticulin and IgM anti-lactoalbumin
- IgM precipitating anti-gluten antibodies in jejunal juice
- Circulating immune complexes
- Atrophy of lymphoreticular tissue (splenic atrophy)



- Impaired blastic transformation of lymphocytes
- Give the endoscopic and histopathological changes of celiac disease
- Endoscopic changes
 - Chromoscopy with methylene blue 1%, indigo-carmin
 - Reduction in number or loss of Kerkring's folds
 - Scalloped fold appearance (transverse linear clefts on the dome when viewed tangentially)
 - Mosaic pattern (geometric reticular pattern)
 - Visible vascular pattern
- Histopathological changes
 - Atrophic mucosa - cuboidal degenerating epithelial layer
 - Crypt hyperplasia
 - Lympho-plasmocytic infiltration of lamina propria
 - Flat mucosa extending over variable length of small bowel up to terminal ileum
 - Paneth cell deficiency
 - Gastric surface mucus cell metaplasia
 - Ulceration and fibrosis (ulcerative jejunoileitis)
 - Brown pigmentation of muscle cells due to vitamin E deficiency
 - Subepithelial collagen deposition

Celiac Disease (Gluten Enteropathy): Grading

Grade I : Intraepithelial lymphocytosis (>30/100 enterocytes)

Grade II : Intraepithelial lymphocytosis and crypt hyperplasia

Grade IIIa : Partial villous atrophy

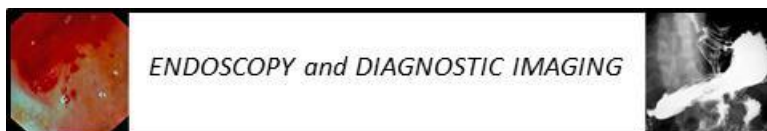
IIIb : Subtotal villous atrophy

IIIc : Total villous atrophy

Grade IV : Irreversible hypoplastic/atrophic changes

➤ Extra-Intestinal Findings

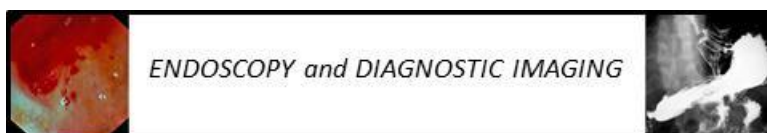
- Chronic mesenteric lymphadenitis and chyladenectasis
 - Replacement of lymphatic tissue by hyaline and fibrous bands
 - Massive lipid accumulation
- Steatosis, hepatocellular damage, centrilobular fibrosis of the liver
- Various degrees of interlobular pancreatic fibrosis and atrophy due to severe nutritional deficiency
- Splenic atrophy in longstanding disease → hyposplenism (Howell-Jolly bodies)
- Skin pigmentation due to melanin deposition in basal layers



- Give the conditions other than celiac disease that may be associated with small bowel total villous atrophy
 - Chronic enteric infections
 - Tropical sprue
 - Bacterial overgrowth
 - Cow milk intolerance
 - Soy protein intolerance
 - Eosinophilic enteritis
 - Immunoglobulin deficiencies
 - Kwashiorkor
 - Malignant lymphoma
 - Collagenous spue
 - Whipple disease
 - Giardiasis
- Give the clinical manifestations which suggest the development of lymphoma in a patient with celiac sprue
 - Return of symptoms after initial response to treatment
 - Deterioration without response to gluten-free diet
 - Fever
 - Skin rash
 - Abdominal pain
 - Palpable abdominal mass
 - Intestinal perforation
 - Intestinal obstruction
 - Hepatosplenomegaly

Recent Updates

- Enteroscopy
- Recent Updates: Celiac Disease
 - Growth failure may occur in children with undiagnosed celiac disease, and catch-up growth may be incomplete after introducing a gluten-free diet. Anti-pituitary antibodies (APA) occur in 42% of newly diagnosed celiac youths (30% high and 70% low titer of APA), and may also be associated with low level of IGF-1 (Devecchio et al, AJG 2010; 105: 691-6).
 - In Europe, the standard mortality rate of persons with symptomatic celiac disease is increased and varies from 1.26 in Finland to 3.6 in Sicily (Biagi & Corazza, 2010).
 - The rate of complete enteroscopy is three times higher with double than with single balloon enteroscopy (66% vs 22%) (May et al., 2010; 105: 575-81).

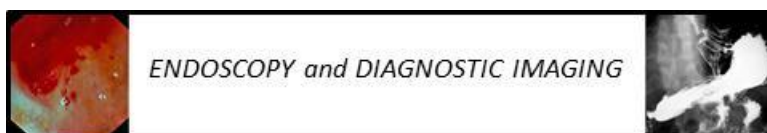


MISCELLANEOUS TUMORS

- Classify the submucosal non-epithelial tumors of the GI tract

Mesenchymal	Benign	Malignant
➤ Stroma Cell	○ Benign GI stroma cell tumor	- Malignant GI stroma cell tumour
➤ Smooth muscle cell	○ Leiomyoma ○ Glomus tumor	- Leiomyosarcoma
➤ Neurogenic	○ Schwannoma ○ Neurofibroma ○ Granular Cell tumor	- Malignant Schwannoma
➤ Lipomatous	○ Lipoma ○ Lipomatosis	- Liposarcoma
➤ Fibrogistiocytic	○ Fibrous Histiocytoma ○ Desmoid tumour ○ Inflammatory pseudotumor ○ Langerhans-cell histiocytosis	- Malignant fibrous histiocytoma - Fibrosarcoma
➤ Endothelial/vascular	○ Hemiangioma ○ Arteriovenous malformation ○ Lymphangioma ○ Hemangio-endothelioma	- Angiosarcoma - Kaposi-sarcoma
➤ Lymphoid	○ Focal/diffuse lymphoid Hyperplasia	- Malignant (B/T cell) lymphoma - Secondary non-Hodgkin leukemia
➤ Lymphoma		

“....For the secret of the care of the patients is in the caring for the patient”
(Peabody, F. W. (1881-1927). The care of the patient. JAMA 1927; 88: 877-82.



Practice Pointers:

➤ Criteria for Malignancy of GI Stroma-cell tumors

	Benign	Borderline malignant	Malignant
○ Diameter in cm	<5	<5	>5
○ Mitotic Activity	<2	>2/<5	>5
○ Proliferative activity in %	<10	<10	>10

➤ Therapeutic possibilities for

○ Leiomyoma:

- Surgical enucleation 66%
- Partial resection 21%
- Endoscopic polypectomy 9%
- Segmental resection 6%

○ Leiomyosarcoma: Therapeutic Possibilities

- Chemotherapy 54%
- Non-resectable 42%
- Radiotherapy 30%
- Partial resection 24%
- En bloc resection 24%
- Enucleation 6%

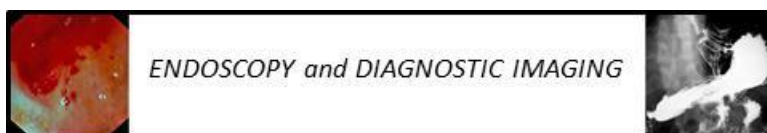
Practice Pointers: Neurofibromatosis

➤ Defining Features

- Multiple café-au-lait spots, often with axillary freckling
- Multiple neurofibromas
- Lisch nodules (pigmented iris hamartomas)

➤ Common or Characteristic Features

- Macrocephaly
- Central-nervous system tumors
 - Optic gliomas
 - Astrocytomas, acoustic neuromas, meningiomas or neurilemmomas
- Segmental hypertrophy
- Cerebrovascular compromise
- Pseudoarthrosis
- Kyphoscoliosis
- Short stature
- Premature or delayed puberty
- Malignant disease



- Neurofibrosarcoma or malignant schwannoma
- Pheochromocytoma
- Intellectual handicap (school-performance problems)
- Speech impediment
- Headache
- Cerebrovascular compromise
- Hypertension
- Constipation
- Visceral neurofibromas
- Pruritus
- Seizures
- Psychosocial burden

Practice Pointers: Characteristics of Functional Duodenal and Upper Jejunal Carcinoids

- Well-differentiated tumor (carcinoid)
 - Benign behaviour: non-functioning, confined to mucosa-submucosa, non-angioinvasive, ≤ 1 cm in size,
 - Gastrin-producing tumor (proximal duodenum)
 - Serotonin-producing tumor
 - Gangliocytic paraganglioma, any size and extension
- Uncertain behaviour: confined to mucosa-submucosa, >1 cm in size and/or angioinvasion
 - Somatostatin-producing tumor, non-functioning (ampullary region), with or without Recklinghausen disease
 - Gastrin-producing tumor, functioning (gastrinoma) or non-functioning, sporadic or MEN-1 associated
 - Serotonin-producing tumor, non-functioning
- Well-differentiated endocrine carcinoma (malignant carcinoid)
- Low-grade malignant: extending beyond submucosa or with metastasis
 - Gastrin-producing carcinoma, functioning (gastrinoma), sporadic or MEN-1 associated
 - Somatostatin-producing carcinoma (ampullary region) with or without Recklinghausen disease
 - Serotonin-producing carcinoma, non-functioning or functioning (any size or extension) with carcinoid syndrome
 - Malignant gangliocytic paraganglioma
- Poorly differentiated endocrine carcinoma
- High grade malignant (small to intermediate cell) carcinoma (ampullary region)



Practice Pointers: Lower Jejunal and Ileal Carcinoids

- Well-differentiated endocrine tumor (carcinoid)
 - Benign behaviour: non-functioning, confined to mucosa-submucosa, non-angioinvasive, ≤ 1 cm in size
 - Serotonin-producing tumor
 - Enteroglucagon-producing tumor
 - Uncertain behaviour: non-functioning, confined to mucosa-submucosa, > 1 cm in size or angioinvasive
 - Serotonin-producing tumor
 - Enteroglucagon-producing tumor
- Well-differentiated endocrine carcinoma (malignant carcinoid)
 - Low-grade malignant: deeply invasive (muscularis propria or beyond) or with metastases
 - Serotonin-producing carcinoma with or without carcinoid syndrome
- Poorly differentiated endocrine carcinoma
 - High grade malignant (small to intermediate cell) carcinoma (rare)

Practice Pointers: Colonic and Rectal Carcinoids

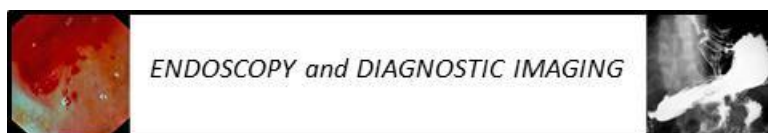
- Well-differentiated endocrine tumor (carcinoid)
 - Benign behaviour: non-functioning, confined to mucosa-submucosa, non-angioinvasive, < 2 cm in size,
 - Enteroglucagon-producing tumor
 - Serotonin-producing tumor
 - Uncertain behaviour: non-functioning, confined to mucosa-submucosa, ≥ 2 cm in size or angioinvasive
 - Enteroglucagon-producing tumor
 - Serotonin-producing carcinoma with or without carcinoid syndrome
- Well-differentiated endocrine carcinoma (malignant carcinoid)

Low-grade malignant:

 - Enteroglucagon-producing carcinoma
 - Serotonin-producing carcinoma with or without carcinoid syndrome
- Mixed exocrine-endocrine carcinoma

High grade malignant (small to intermediate cell) carcinoma
- Mixed exocrine-endocrine carcinoma

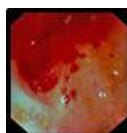
Moderate to high grade malignant
- Lymph node metastases
 - Size
 - < 1 cm tumor size (2%)



- 1.0-2 cm tumor size (10%)
- >2 cm tumor size (80%)

Practice Pointers: Appendiceal Carcinoids

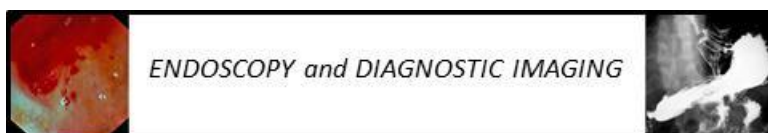
- Well-differentiated tumor (carcinoid)
 - Benign behaviour: non-functioning, confined to appendiceal wall, non-angioinvasive, < 2 cm in size
 - Serotonin-producing tumor
 - Enteroglucagon-producing tumor
 - Uncertain behaviour: non-functioning, confined to subserosa, ≥ 2cm in size or angioinvasive
 - Serotonin-producing tumor
 - Enteroglucagon-producing tumor
- Well-differentiated endocrine carcinoma (malignant carcinoid)
 - Low-grade malignant: invading the mesoappendix or beyond or with metastasis
 - Serotonin-producing carcinoma with or without carcinoid syndrome
- Mixed exocrine-endocrine carcinoma
 - Low grade malignant:
 - Goblet cell carcinoid
- Carcinoid Syndrome
 - Occurs in <10% of carcinoid tumors
 - 3.2 cases per 1,000,000
 - Oversecretion of peptides and hormones
 - Serotonin - kalikrein/bradykinin – prostaglandins
 - Tachykinins - histamine
 - Sign of advanced disease
 - Occurrence and severity vary by tumor size, site and degree of metastasis
 - Syndrome is associated with metastasis and high blood levels of secreted hormones
 - Manifestations
 - Skin: Flushing, telangiectasias and pellagra-like dermatitis
 - GI: Diarrhea and abdominal cramps
 - Heart: Fibrosis of the right-sided endocardium leading to tricuspid and pulmonic valvular stenosis and insufficiency
 - Lungs: Bronchoconstriction

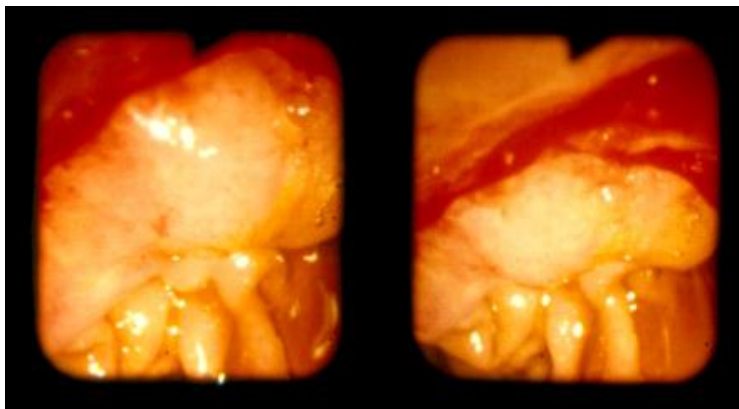




- Clinicopathologic Classification of Endocrine Tumors of the Duodenum and Upper Jejunum
 - Well-differentiated tumor (carcinoid)
 - Benign behaviour: non-functioning, confined to mucosa-submucosa, non-angioinvasive, ≤ 1 cm in size,
 - Gastrin-producing tumor (proximal duodenum)
 - Serotonin-producing tumor
 - Gangliocytic paraganglioma, any size and extension
 - Uncertain behaviour: confined to mucosa-submucosa, >1 cm in size and/or angioinvasion
 - Somatostatin-producing tumor, non-functioning (ampullary region), with or without Recklinghausen disease
 - Gastrin-producing tumor, functioning (gastrinoma) or non-functioning, sporadic or MEN-1 associated
 - Serotonin-producing tumor, non-functioning
 - Well-differentiated endocrine carcinoma (malignant carcinoid)
 - Low-grade malignant: extending beyond submucosa or with metastasis
 - Gastrin-producing carcinoma, functioning (gastrinoma), sporadic or MEN-1 associated
 - Somatostatin-producing carcinoma (ampullary region) with or without Recklinghausen disease
 - Serotonin-producing carcinoma, non-functioning or functioning (any size or extension) with carcinoid syndrome
 - Malignant gangliocytic paraganglioma

- Poorly differentiated endocrine carcinoma
 - High grade malignant (small to intermediate cell) carcinoma (ampullary region)
- Carcinoid Syndrome
 - Oversecretion of peptides and hormones
 - Serotonin
 - Tachykinins
 - Sign of advanced disease
 - Occurs in <10% of carcinoid tumors
 - 3.2 cases per 1,000,000
 - Occurrence and severity vary by tumor size, site, and degree of metastasis
 - Syndrome follows metastasis and high blood levels of secreted hormones
- Clinicopathologic Classification of Endocrine Tumors of the Lower Jejunum and Ileum
- Well-differentiated endocrine tumour (carcinoid)
 - Benign behaviour; non-functioning, confined to mucosa-submucosa, non-angioinvasive, ≤ 1 cm in size,
 - Serotonin-producing tumor
 - Enteroglucagon-producing tumour
 - Uncertain behaviour: non-functioning, confined to mucosa-submucosa > 1 cm in size or angioinvasive
 - Serotonin producing tumour
 - Enteroglucagon producing tumour
- Well-differentiated endocrine carcinoma (malignant carcinoid)
 - Low-grade malignant: deeply invasive (muscularis propria or beyond) or with metastases
 - Serotonin-producing carcinoma with or without carcinoid syndrome
- Poorly differentiated endocrine carcinoma
 - High grade malignant (small to intermediate cell) carcinoma (rare)





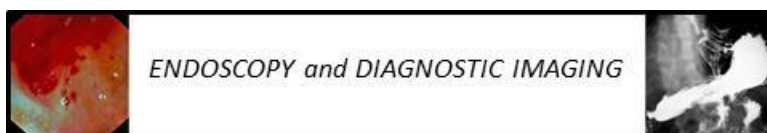
FISTULAE

Different schemes for the classification of any type of gastrointestinal fistulae, based on anatomy, output volume, and etiology.

Scheme	Classification
➤ Anatomical	Internal, external Low, high Simple, complex
➤ Output volume	Pancreatic Low (<200 ml/day) High ($\geq$ 200 ml/day) Intestinal Low (<500 ml/day) High ($\geq$ 500 ml/day)
➤ Etiological	Underlying disease

Printed with permission: Messmann H, et al. *Best Practice & Research Clinical Gastroenterology* 2004, pg. 811.

- Give the patient-related and fistula-related characteristics associated with spontaneous closure of any kind of GI fistulae.
- Patient characteristics
 - Output (mL/day) <500
 - Age (yr) <40
 - Nutritional status – well nourished
 - Cause
 - Anastomosis characteristics – anastomotic breakdown
- Fistula characteristics

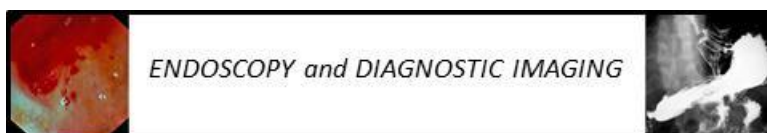


- Lateral fistula
- No incomplete disruption
- No abscess near leakage
- No distal obstruction
- Fistula tract >2 cm
- Non-epithelialized fistula tract
- Enteral defect <1 cm
- Fistula site: Oropharyngeal, esophageal, duodenal stump, pancreatobiliary, jejuna
- Late post operative leakage
- Adjacent bowel healthy
- No severe systemic diseases

Printed with permission: Messmann H., et al. *Best Practice & Research Clinical Gastroenterology* 2004, pg. 812.; and Hoffman KM, Furukawa M, Jensen RT. *Best Practice & Research Clinical Gastroenterology* 2005; 19(5): pg 677.

CROHN DISEASE

- Give the classification, diagnostic tests, and medical and/or surgical treatments for patient with Crohn disease (CD) and perianal fistulae (PF)
- Classification – low, high; simple, complex; anatomic position
- Diagnostic tests
 - Digital rectal examination (DRE)
 - EUA (examination under general anesthesia)
 - Pelvic ultrasound
 - Pelvic CT
 - Pelvic MRI
 - Sigmoidoscopy/colonoscopy
 - EUS
 - Barium studies (fistulogram sonogram)
 - Cystoscopy
- Treatments
 - Medical
 - Drugs used to treat Crohn disease
 - CO₂ laser ablation
 - Hyperbaric O₂
 - Injection of silver microspheres with antibiotic
 - Surgery
 - Seton placement
 - Glue
 - Fistulotomy



- Endorectal advancement flap
- Fecal diversion
- Proctocolectomy

Abbreviations: CD, Crohn disease; DRE, digital rectal examination; EUA, examination under general anesthesia; EUS, endoscopic ultrasound; PF, perianal fistulae

➤ Anal Fissures

- Often multiple, also located laterally or centrally
- Often wide with undermined edges
- Limited pain, lack of reactive sphincter spasm
- Covered with indurated firm cap-like skin fold
- Reddish violet edematous perianal skin with radial pronounced furrows
- Limited tendency to healing

➤ Perianal Fistulas

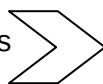
- 20–30 % of patients with CD has fistulas
- Decreased quality of life
- 50% of patients with Crohn colitis and perianal fistula's end with ileostomy
- Few effective therapeutic approaches

➤ Pro-inflammatory Cytokines in CD

- Cytokines are key mediators in a variety of inflammatory processes and diseases
- Antigen-stimulated T-cell activation stimulates release of TNFa
- TNFa is a key cytokine in the inflammatory cascade and regulates the production of other pro-inflammatory cytokines

➤ Key actions attributed to TNFa

- Macrophages
 - Increased pro-inflammatory cytokines
 - Increased chemokines
- Endothelium
 - Increased adhesion molecules → increased cell infiltration
 - Increased acute phase response → increased CRP in serum
- Fibroblasts
 - Increased metalloproteinase synthesis
 - Increased collagen production
- Epithelium
 - Increased ion transport
 - Increased permeability



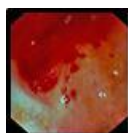
Increased
Inflammation



Tissue
remodelling



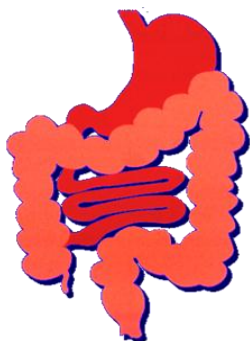
Compromised
barrier function



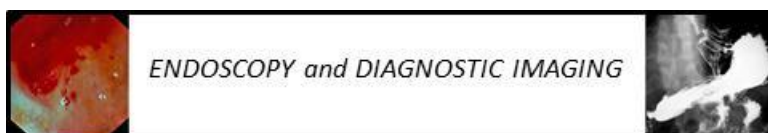
ENDOSCOPY and DIAGNOSTIC IMAGING



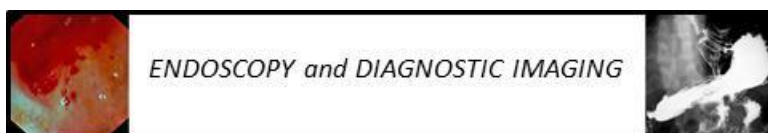
- Role of TNF α and IL-1 in Acute Inflammation
 - Amplify immunologic and inflammatory processes
 - Enhance cellular catabolism
 - Induce acute phase proteins
 - Induce pyrogenic activity
 - Stimulate PGI₂, PGE₂, and PAF secretion
 - Activate endothelial cells and induce IL-1 (TNF α)
- Nuclear Factor Kappa B
 - Potent regulator of inflammation gene transcription
 - Pro-inflammatory stimuli (ie TNF, LPS) activate NF κ B
 - IL-10 and steroids reduce the amount of activated NF κ B
- Give the clinical presentation to ulcerative colitis (UC), the differential diagnosis, the endoscopic and histopathological changes.
 - Bloody diarrhea
 - Abdominal cramping
 - Tenesmus
 - Weight loss
 - Systemic symptoms
 - Extraintestinal manifestations
 - Symptoms depend on extent and severity of inflammation
- Give the presentation of Crohn disease, the causes of diarrhea, serological test, factors leading to malnutrition, histopathological changes, diagnostic imaging, colonoscopy, differential diagnosis.
- History
 - Diarrhea
 - Chronic abdominal pain and tenderness
 - Weight loss
 - Fever
 - Perianal disease
 - Symptoms vary with location of disease
 - Extraintestinal manifestations



- Esophagus <1%
- Stomach 6%
- Duodenum 5%
- Right colon 68%
- Small bowel 3%
- Terminal Ileum 37%
- Rectum 20%



- Different Causes of Diarrhea in Crohn disease
 - Active disease
 - Small intestinal bacterial overgrowth
 - Bile salt malabsorption after ileal resection
 - Hypolactasia
 - Short bowel after resection
 - Other disease (celiac, chronic pancreatitis)
 - Co-existent irritable bowel syndrome
- Conditions that cause “colitis” and may mimic UC.
 - Infection
 - Viral
 - Cytomegalovirus (CMV)
 - Herpes (HSV)
 - Bacterial
 - Clostridium difficile
 - Salmonella species
 - Shigella species
 - Yersinia enterocolitica
 - Campylobacter jejuni
 - Vibrio perahaemolyticus
 - Aeromonas hydrophila
 - Neisseria gonorrhoeae
 - Listeria monocytogenes
 - Chlamydia trachomatis
 - Syphilis
 - Staphylococcus aureus
 - Escherichia coli 0157:H9
 - Protozoan
 - Amebiasis (ENT amoeba histolytica)
 - Balantidiasis
 - Schistosomiasis
 - Fungal
 - Histoplasmosis
 - Candidiasis
 - Iatrogenic (drugs)
 - Enemas
 - Laxatives
 - Ergotamine
 - Amphetamines
 - Phenylephrine
 - Cocaine
 - Nonsteroidal anti-inflammatory drugs (NSAIDs)
 - Penicillamine
 - Gold



- Methyldopa

Abbreviations: CMV, cytomegalovirus; HSV, herpes simplex virus

Adapted from: Su C, and Lichtenstein G R. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006. pg.2514.

- Factors that Lead to Malnutrition in IBD
 - Decreased oral intake
 - Increased caloric requirements
 - Malabsorption of nutrients
 - Loss of proteins and electrolytes
 - Drug-induced nutritional complications
 - Down regulation of metabolism by pro-inflammatory cytokines
- Pathology: Biopsy features of acute self-limiting colitis (AC) which help to distinguish it from chronic idiopathic ulcerative colitis (UC):
 - Crypts are straight, parallel, close
 - No lymphoplasmacytosis at base of crypts
 - Large, bulging, cystic dilation with a “necklace” of cells around any crypt abscess
 - PML are abundant, and scattered in the lamina propria (LP)

Abbreviations: AC, acute self-limiting colitis; LP, lamina propria; PML, polymorphonuclear leucocytes; UC, ulcerative colitis

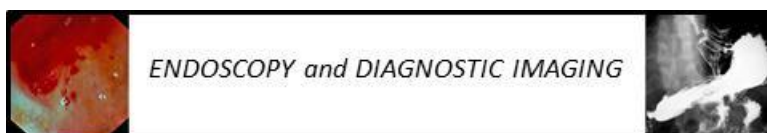
- Indications for Surgical Treatment in Crohn disease
 - Recurrent bowel obstruction
 - Complicated fistulae
 - Abscess
 - Failure or complications of medical therapy
 - Perianal complications
 - Toxic megacolon
 - Growth retardation in children



Surgeries in CD Procedures	Indications
Resection and anastomosis	- Regional enteritis, ileocolitis, segmental disease
Strictureplasty	- Multiple segmental strictures in jejunoileitis, - Proximal skip disease (in conjunction with resection)
Colectomy and ileostomy	- Pan(ileo)colitis with rectal involvement, severe perirectal sepsis
Subtotal and total colectomy	- Extensive colitis with normal rectum and ileoproctostomy
Temporary ileostomy	- Alternative to anastomosis when anastomosis or colostomy not appropriate

- Give the causes, diagnostic procedures, and the managements for a patient with Crohn disease (CD) who presents with sub-acute, small bowel obstruction (SBO), give the.

- Causes
 - Active CD
 - Stricture
 - Fruit pits
 - Gallstone ileus
 - Enterolith
 - Endometriosis
- Differential Diagnosis of CD
 - Lymphoma
 - Infectious etiologies
 - Appendicitis
 - Diverticulitis
 - Carcinoma
 - UC
 - Celiac disease
- Diagnostic procedures
 - Plain abdominal films
 - Conventional CT
 - CT enterography
 - Small bowel (gastrograffin) x-ray
 - Abdominal ultrasound
 - Doppler ultrasound
 - MRI enterography

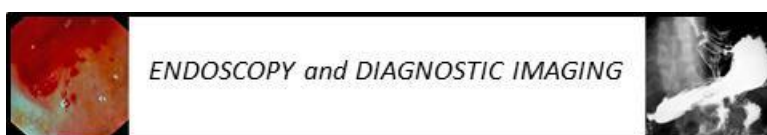


- FDG-PGT (18F- flurodeoxyglucose positron emission tomography [PET])
- Capsule endoscopy (penalty, because of suspected stricture)
- Management
 - Treatment of inflammatory CD (avoid anti-TNF)
 - Through-the-scope balloon dilation
 - Adjuvant steroid injection into narrowing
 - Expandable metal stents
 - Stricturoplasty
 - Open or laparoscopic surgical resection

Abbreviations: CD, Crohn disease; PET, positron emission tomography; SBO, small bowel obstruction

DIARRHEA

- Give a classification of drugs used in GI which are commonly associated with diarrhea.
 - Esophagus/stomach
 - Mg-containing antacids, PPIs, H2RAs
 - Misoprostol
 - Small bowel
 - Prokinetics
 - Antiabsorptives
 - 5-ASA, immunosuppressants
 - Colon
 - Laxatives osmotic
 - Mag citrate
 - Antibiotics
 - Cholinergics
 - Liver
 - Lactulose (PSE)
 - Herbs
 - Heart
 - Beta blockers
 - Chemotherapy
- Give the causes of prolonged diarrheal illness after travel (“prolonged traveller’s diarrhea”).
 - Infection
 - Persistent bacterial infection
 - Missed second infection



- Aeromonas
 - Escherichia coli (enteroinvasive)
 - Persistent protozoal infection
 - Giardia
 - Entamoeba histolytica
 - Cryptosporidium
 - Antibiotic-associated colitis
 - Onset of chronic (presumably viral) enteritis/colitis
- Diet/Drugs
- Change in diet
 - Excess alcohol intake
 - Drugs
- Other Diseases
- Unmasked lactase deficiency, GSE, IBD, IBS, lymphocytic/collagenous colitis
 - Tropical sprue
 - Post-infectious diarrhea-predominant IBS (D-IBS)

Abbreviations: D-IBS, diarrhea-predominant IBS; GSE, gluten sensitive enteropathy; IBD, inflammatory bowel disease; IBS, inflammatory bowel syndrome.

- Give the causes of protein-losing enteropathies.
- Increased lymphatic pressure
- Congestive heart failure
 - Constrictive pericarditis
 - Primary, secondary lymphangiectasia
- Ulcerating intestinal disease
- IBD (Crohn disease, ulcerative colitis)
 - Colon cancer
- “Leaky gut”
- Celiac disease
 - Small intestinal bacterial overgrowth
 - Whipple’s disease
 - Vasculitides
- Factors/approaches that have been shown to enhance recovery from postoperative ileus.
- Thoracic epidural local anesthetics
 - Intravenous or wound local anesthetics
 - Laxatives

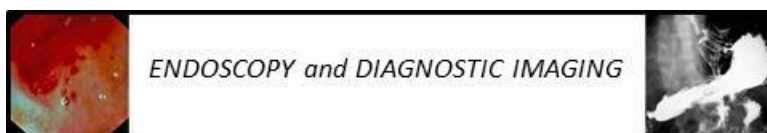


- Peripheral opioid antagonists
- Goal-directed fluid therapy and avoiding fluid excess
- Early oral feeding
- Laparoscopic surgery
- Chewing gum
- Avoid NG tubes
- Minimize opioid use

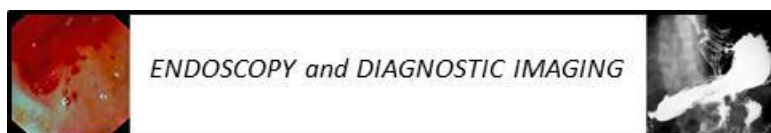
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Diagnostic imaging

- Inflammatory and ulcerative diseases
 - Peptic ulcer disease
 - Zollinger – Ellison syndrome (ZES)
 - Pancreatitis
 - Crohn disease
 - Celiac disease (gluten sensitive enteropathy)
- Filling defects
 - Benign tumors
 - Polyps
 - Pseudopolyp
 - GIST
 - Lipoma
 - Malignant tumors
 - Adenocarcinoma
 - Lymphoma
 - GIST
 - Metastases
 - Ampullary carcinoma
 - Non-neoplastic lesions
 - Heterotopic gastric mucosa
 - Brunner gland hyperplasia
 - Enteric duplication cyst
 - Annular pancreas
 - Intraluminal diverticulum
- Miscellaneous
 - Diverticulum
 - Aortoenteric fistula
 - Perforation
- Narrowing



- Benign
 - Peptic ulcer disease
 - Pancreatitis
 - Crohn disease
 - Hematoma
 - Superior mesenteric artery syndrome
 - Annular pancreas
 - Malignant
 - Adenocarcinoma
 - Lymphoma
 - GIST
 - Metastases
 - Ampullary carcinoma
- Thickened folds
- Benign
- Peptic ulcer disease
 - Zollinger – Ellison syndrome
 - Brunner gland hyperplasia
 - Pancreatitis
 - Crohn disease
 - Celiac disease
 - Whipple disease
 - Hematoma
 - Cystic fibrosis
- Malignant
- Lymphoma
- Filling defects
- Adenocarcinoma
 - Narrowing, apple- core, polypoid mass
 - Eccentric
 - Loss of mucosal markings
 - Usually distal to ampulla
 - Irregular surface
 - CT short segment wall thickening
 - Cannot be distinguished radiologically from metastases
 - Lymphoma
 - Bulky mass
 - Ulceration
 - Solitary
 - GIST
 - Smooth surface (extramucosal)



- Calcification (suggestive of smooth muscle tumors)
- Central necrosis
- Periapillary adenocarcinoma
 - Head of pancreas - Duodenum
 - Narrow
 - Distorted
 - Ulcerated
 - “reverse 3 (epsilon) sign”
 - Body / tail of pancreas mass indentation of gastric body / fundus
- Polyp villous adenoma
 - Cauliflower – like surface of mass
 - Barium fills small indentations in surface

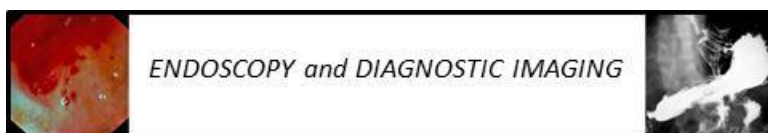
Distinguishing diagnosis: multiple, duodenal filling defects

- Fundic gland polypoidosis syndrome (FAP)
- Gastric polyps hyperplastic
- Duodenal polyps adenomatous

- Heterotropic gastric mucosa
 - Filling defects – tiny
 - Multiple – angular
- Nodular lymphoid hyperplasia
 - Round
 - Small
 - Uniform
 - Distributed diffusely, evenly
- Brunner gland hyperplasia
 - Varying size
 - Large
- Flexural pseudopolyp
 - Remnant mucosa at the junction of first and second part of duodenum
- Prolapsing gastric polyps
 - Fluoroscopy needed to show prolapsed of polyps from stomach
 - Duodenal polyps do not prolapse into stomach
- Enteric duplication cyst
 - Mass
 - Smooth surface (extramucosal – extrinsic)
 - Indents duodenal wall

➤ Narrowing

- Annular pancreas
 - Gas in the distended stomach and duodenum
 - Gas has “double-bubble” appearance



- Differential diagnosis of duodenal narrowing
 - Annular pancreas
 - Duodenal adenocarcinoma / metastases
 - Pancreatitis
- Miscellaneous
 - Diverticulum
 - Usually medial wall of second portion of duodenum (periampullary)
 - Folds enter the diverticula (but not an ulcer)
 - Intraluminal diverticulum
 - Starts as a diaphragm at or near the papilla of Vater
 - Pressure against the diaphragm produces the intraluminal diverticulum
 - The diverticulum develops into a sac-/ balloon – like structure
 - A radiolucent band surrounds the sac-like structure (the wall of the diverticulum)
 - With pancreatitis, the diaphragm → diverticulum may develop

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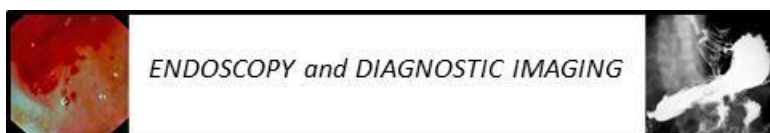
Distinguishing diagnosis: dilation of proximal small bowel / duodenum

- Superior mesenteric artery (SMA) syndrome
 - AAA (abdominal aortic aneurysm)
 - Duodenal neoplasia
 - Pancreatitis
-

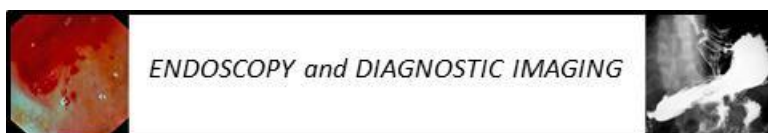
- SMA syndrome
 - Sudden narrowing of 3rd portion of duodenum (D3) by SMA anteriorly and posteriorly the spine and aorta
 - Linear extrinsic “mass” (SMA)
 - Proximal (D1/ D2) dilation
 - Mucosa in D1/D2 is normal
 - Retroperitoneal duodenal perforation
 - Non’specific signs\retroperitoneal air
 - Loss of psoas shadow
 - Segmental ileus
 - Stranding of soft tissue
 - Leakage of contrast material

➤ Filling defect / narrowing

- Hematoma
 - Mass effect
 - Thickened folds (like a “stack of coins”)



- Narrowing
 - Smooth
 - scalloped
- Pyloric torus defect (niche)
 - long, narrow pyloric channel
 - mucosal prolapse (between the two muscle bundles that form the pylorus and converge towards the lesser curve of stomach)
 - triangular collection of contrast in the pylorus (“niche”)
 - differential diagnosis of niche in pyloric channel
 - ulcer
 - carcinoma
 - adult pyloric stenosis
- Filling Defects
 - Benign Tumors
 - Polyp
 - Gist
 - Lipoma
 - Hemangioma
 - Malignant Tumors
 - Adenocarcinoma
 - Lymphoma
 - Gist
 - Carcinoma
 - Metastases
 - Non-neoplastic Lesions
 - Gallstone ileus
 - Duplication cyst
 - Ascariasis
- GIST
 - Benign
 - Submucosal / subserosal filling defect
 - Mass / polyp
 - CT – increased vascularity
 - Malignant
 - Dumbbell-shaped
 - Ulcerating mass
 - Intraluminal filling defect
 - Intramural



- Cavitating mass

Distinguishing diagnosis : multiple filling defects

- Lymphoma
- Hemangioma
- Neurofibroma
- Metastases
- Multiple intestinal polyposis
- Polyposis syndrome

➤ Lipoma

- Smooth – surface filling defect usually single
- CT-homogeneous fatty attenuation
- No soft tissue density

Distinguishing diagnosis : lipoma

- Liposarcoma
 - heterogeneous fat density
 - soft tissue in tumor

➤ Hemangioma

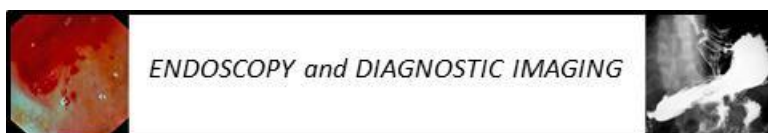
- Focal / diffuse
- Small
- Usually single
- May be calcified

➤ Diffuse hemangiomatosis

- Submucosal / intraluminal filling defects
- Associated with rare syndrome

➤ Hamartomas (Peutz-Jeghers syndrome [PJS])

- Clusters of filling defects (polyp)
- Cauliflower-like polyps
- Often in jejunum
- May be associated with adenomas in colon, stomach, duodenum)



Distinguishing diagnosis: Smooth-surfaced filling defects in small bowel

- Inflammatory fibroid polyp
- GIST
- Lipoma
- Hemangioma

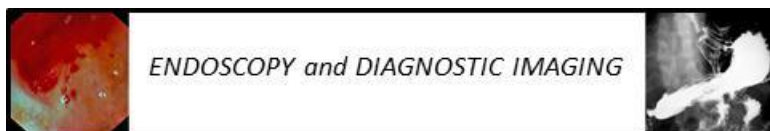
➤ Carcinoid tumor

- Filling defects
- Intramural
- Ulceration of surface
- Fibrotic reaction in the mesentery when tumor spreads through the serosa
 - Obstruction
 - Standing mesentery and desmoplastic reaction (CT)
 - Linear standing outwards from central calcified mass in mesentery ("starburst" pattern).
- Metastases to mesentery
 - Narrowing of lumen
 - Tethering of folds of adjacent bowel
 - Separation of loops of small bowel from mesenteric tumor
- Metastases to liver
 - Increased vascularity
 - Regions of central necrosis

• Lymphoma

➤ non-Hodgkin type

- Multiple nodules
- Polypoid
- Infiltration
 - Focal
 - Loss of mucosal marking (ulceration of mucosa)
 - Narrowing of lumen (fibrotic reaction)
 - Dilation of bowel (no fibrotic reaction)
 - Thickening of folds
- Endo-excentric
- Ulcerating mass
- Fistula
- May involve cecum



Distinguishing diagnosis: Small bowel narrowing

- Focal infiltrative lymphoma
 - Loss of mucosal folds in narrow lumen
- Ischemia
- Amyloidosis
 - Secondary ischemic changes (loss of mucosal folds)
 - Thickening of small bowel folds

➤ Hodgkin Lymphoma

- Narrow lumen
- Long segments
- Ulceration
- Folds
 - Thick
 - Irregular

➤ AIDS-associated (B-cell) lymphoma

➤ CT

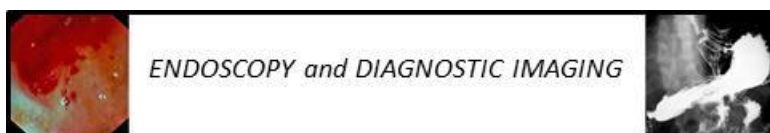
- Large
- Bulky
- Adenopathy

➤ Adenocarcinoma

- Duodenum
- Short
- Annular (“apple-core” lesion)
- Constricting
- Ulcerating (“smudged” appearance)
- May be signs of associated
 - Celiac disease
 - Crohn disease
- Loss of normal mucosal markings
- CT
 - Soft tissue mass
 - Thick wall

➤ Metastases to bowel wall

- Multiple masses
- Single, large mass
- Ulceration
- Intramural (loss of mucosal markings)
- Mesenteric mass



Distinguishing diagnosis: polypoid mass protruding into small bowel lumen (any submucosal tumor)

- Lipoma
- GIST

Distinguishing diagnosis: multiple mass in a single loop of bowel

- Lymphoma
- Metastases

Distinguishing diagnosis: metastasis to the bowel wall, growing into the mesentery and destroying the bowel wall, leading to loss of mucosa

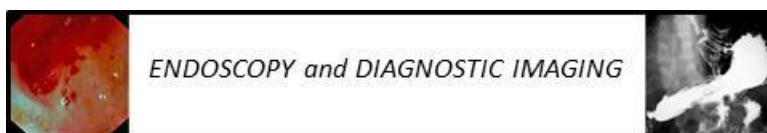
- Lymphoma
- GIST
- Metastases from colon

➤ Metastasis to serosa (intraperitoneal seeding)

- Site
 - Pouch of Douglas
 - Ileocecal region
 - Superior aspect of sigmoid colon
- Primary
 - GI tract
 - Ovaries
- Lumen of small bowel
 - Narrow
- Loops
 - Angulated
 - Kinked
- Folds
 - Thick
 - Tethering (mesenteric retraction)

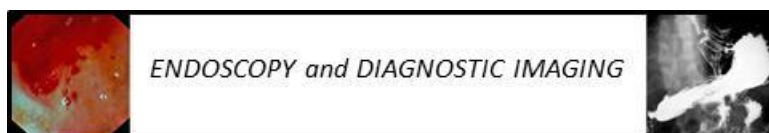
➤ Gallstone ileus

- Triad
 - Mechanical small bowel obstruction

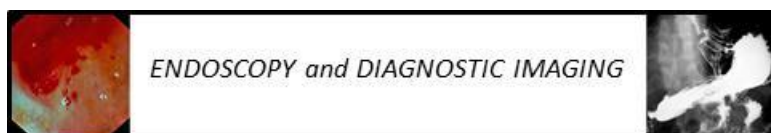


- Ectopic, calcified gallstone at transition point between normal and dilated bowel
 - Air in biliary tree (pneumobilia)
- Site of gallstone erosion
 - Stomach
 - Small bowel
 - Colon
- Ascariasis
 - Thin white line in middle of long filling defect, representing barium ingestion by roundworm
 - Thick mucosal folds
- Segmental / Diffuse Disease: folds (valvulae conniventes) thin/thick, straight / nodular
 - Are the folds abnormal
 - Are the abnormal folds
 - Thin or thick
 - Straight or nodular
 - Segmental or diffuse
 - Classification of folds

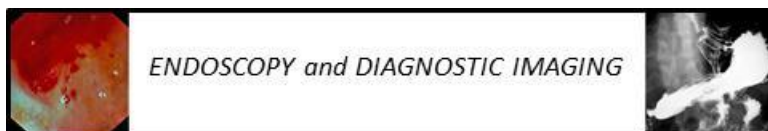
Type I – thin, straight folds	
Type II – thick, straight folds	segmental, or diffuse
Type III – thick, nodular folds	segmental, or diffuse
- Type I
 - Folds
 - Thin (< 3 mm)
 - Straight
 - Lumen-dilated
 - Obstruction
 - Mechanical
 - Motility (ileus)
 - Celiac disease
 - Scleroderma
- Type I folds (thin straight)
 - Obstruction
 - Mechanical
 - Motility (paralytic Ileus)
 - Celiac disease
 - Scleroderma
- Type II folds (thick, straight)
- Segmental



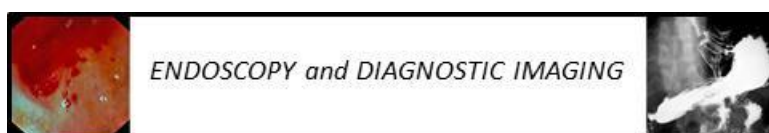
- Ischemia
- Intramural hemorrhage
- Radiation enteritis
- Adjacent inflammation
- Diffuse
 - Hypoproteinemia
- Type III folds (thick, nodular)
- Segmental
 - Nodular lymphoid hyperplasia
 - Lymphoma
 - Crohn disease
 - Metastases
- Mechanical Small Bowel Obstruction
 - Loops dilated (> 3 mm) diameter)
 - Air-fluid levels
 - Loops separated from each other
 - Transition between normal and abnormal part of small bowel
 - Transition forms rounded defect
 - Lack of gas in colon (gas often seen in colon in paralytic ileus)
 - Sudden narrowing between normal and dilated small bowel
 - Smooth rounded defect
 - Lack for ventral abnormal wall hernia
 - Causes
 - Adhesions
 - Hernia's
 - Tumor
 - Intussusception
 - Stricture
 - Crohn disease
 - Ischemia
 - Idiopathic
 - Volvulus
- CT
 - Best test to identify cause of obstruction (75%)
 - Difference in proximal and clustal small bowel suggests mechanical obstruction (in paralytic ileum caliba of jejunum and ileum)
- Volvulus
 - Congenital loss of normal peritoneal attachments
 - Whorl-like CT pattern of small bowel and mesenteric wrapper around the superior mesenteric artery (SMA)
 - Ischemia



- Scleroderma
 - Thin, straight folds
 - Folds stacked closely together
 - Loops dilated
 - Sacculations on anti-mesenteric border of small bowel
 - No hypersecretion (unlike celiac disease)
- Celiac Disease
 - Thin, straight folds
 - Loops dilated
 - Hypersecretion (flocculation of barium)
 - Reversal of normal jejunal and ileal pattern
 - Normal jejunum (> 3 folds per jejunum)
 - Abnormal jejunum ("ilealization"; ≤ 3 folds per inch)
 - "jejunization" of ileum
 - "ilealization of jejunum"
 - Loss of jejunal mucosal marking leaving featureless tubular bowel ("moulage" sign, i.e., molded, casted structure)
 - Strictures (from previous jejunoileitis)
 - Absent
 - Featureless bowel
 - Folds
 - Thickened
 - Stricture (from previous jejunoileitis)
 - Smooth
 - focal
 - Cavitory lymph node system, with hyposplenism
 - Celiac disease plus lymphoma
 - Ulcerating jejunoileitis
 - Multiple ulcers
 - Intussusception (transient)
 - "coiled-spring" appearance
- Diffuse
 - Polyposis syndrome
 - Nodular lymphoid hyperplasia
 - Lymphoma
 - Metastases
 - Whipple disease
 - Lymphangiectasia
 - Eosinophilic gastroenteritis
 - Amyloidosis
 - Mastocytosis



- Type II Folds - Segmental
 - Thick
 - Straight
- Ischemia
 - Often normal early study (50%)
 - Papralytic (adynamic) ileus
 - Isolated, dilated loop
 - Thick mucosal folds
 - Pneumatosis
 - Portal venous gas
- CT
 - Infarction
 - Wall thickening
 - Focal
 - Diffuse
 - Segmental dilation
 - Mesenteric edema
 - Ascites
 - Intramural gas (pneumatosis)
 - Cystic
 - Linear-curvilinear
 - Radiolucent rim along wall of bowel (pathognomonic)
 - Posterior, dependent position
 - Venous gas
 - Mesenteric vein
 - Portal vein
 - More air in non-dependent portal veins, than in the dependent posterior lobe
 - Closed loop obstruction (adhesion traps bowel and causes ischemia in a loop of small bowel)
- Radiation enteritis
 - > 40 Gy (4,000 rad)
 - Endarteritis obliterans
 - Folds
 - Segmental, type I
 - Ischemia, hemorrhage, radiation
 - Diffuse, type II
 - Venous congestion, hypoalbuminemia, cirrhosis
 - Lumen-narrowed
 - Wall-edema (thumbprinting)
 - Stenosis
 - Obstruction (adhesions)
 - Confined to area exposed to radiation



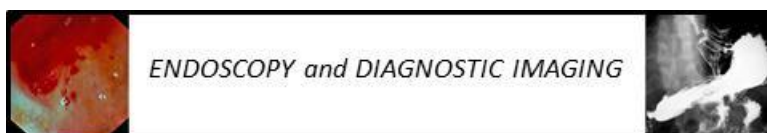
- Type II Folds - Diffuse
 - Thick (> 3 mm)
 - Straight
- Hypoproteinemia
 - Cirrhosis, nephrotic syndrome, CHF
 - Diffuse thickening of wall (diffuse edema of mesentery)
 - Diffuse increased density of mesentery on CT (edema of mesentery)
 - Diagnostic imaging changes of portal hypertension, chronic
 - Renal failure, congestive heart disease
- Type III Folds
 - Thick nodular folds
 - Segmental
- Nodular Lymphoid Hyperplasia (NLH)
 - Small (< 4 mm) nodular lesions
 - Similar size/shape
 - Umblicated nodules (like an aphthoid ulcer)
 - Irregular contour of bowel wall
 - Inflammation
 - Thick folds
 - Inflammation
 - Rapid transit
 - Spasm
 - May have “jejunization” of ileum (> 3 folds per inch of ileum)
 - Associated with infection (eg., giardiasis)
 - Hypogammaglobulinemia

.....

Differential diagnosis: NLH vs. Lymphoma

- Lymphomatous nodules
 - Large
 - Varying size / shape
 - Ulceration (not just umblication)
-

- Lymphoma
 - Submucosal
 - Non-specific nodular thickened folds
 - Nodules of varying size
 - Long segments (diffuse) or multiple focal lesions
 - Affects any portion of bowel
 - Mesenteric lymphadenopathy
 - Celiac disease plus lymphoma



➤ Metastases

- Multiple
- Larger nodules (> 4 mm)
- Affects any portion of small bowel
- Diffuse (not segmental like crohn disease)
- With or without ulceration
- Differential diagnosis
 - Thick (> 4 mm), nodular folds
 - Multiple
 - Diffuse
- Lymphoma
- Lymphangiectasis
- Peutz-Jeghers polyps
- Metastases

➤ Amyloidosis (systemic)

- Submucosal amyloid
- Thick nodular folds
- Atrophic folds
- Polypoid protrusions
- Dilation

➤ Whipple Disease

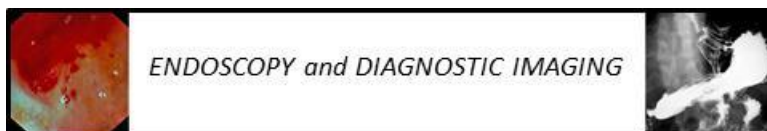
- Folds
 - Thick
 - Nodular
 - Jejunum (localized)
- No sprue-like findings
 - Diffuse
 - Dilation
 - Flocculation (hypersecretion)
- CT
 - Lymphadenopathy (may be just mesenteric lymphadenopathy)
 - Fatty deposition (low attenuation)

.....
 Distinguishing diagnosis: Whipple disease

- Mycobacterium avium-intracellular (MAC)
 - Giardiasis
 - Cryptosporosis
-

➤ Eosinophilic Gastroenteritis

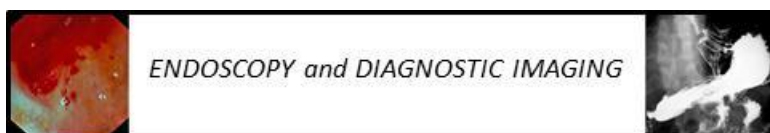
- Stomach-localized
- Small bowel-diffuse
- Thick, nodular folds (non-specific)
- Narrow lumen



- Wall-rigid
- Intestinal lymphangiectasia
 - Thick, nodular folds (> 4 mm, nonspecific)
 - Nodular filling defects of different sizes
 - Smaller large filling defects
 - Increase secretion (increased fluid in lumen)
 - Affects any portion of the bowel
 - Diffuse
- Crohn disease
 - Thick, nodular folds
 - Aphthous ulcers
 - Multiple ulcers
 - Long / serpiginous ulcers (aphthous / multiple ulcers coalesce, forming longitudinal / transverse ulcerations)
 - Mucosa cobblestoned
 - Wall thickened
 - Edema
 - Inflammation
 - Fibrosis
 - Lumen narrowed / dilated (transmural fibrosis with proximal dilation)
 - Stricture
 - Irregular
 - Asymmetrical
 - May be circumferential
 - Short / long ("string sign")
 - Skip areas
 - Fibrosis
 - Ulcers
 - Transmural inflammation
 - Fistulae
 - Abscesses (may be in wall or between loops of bowel ("interloop"))

.....
 • Distinguishing diagnosis: indistinguishable from Crohn disease
 • (erosions, fold thickening, strictures)
 •

- Tuberculosis
 - Actinomycosis
 - Histoplasmosis
 - Blastomycosis
-



- Similar to Crohn disease (erosions, fold thickening, strictures)
 - Yersinia
 - Salmonella
- CT
 - Segmental thickening
 - Homogeneous (soft tissue), or heterogeneous (soft tissue and water ["water-density" ring])
 - Mass
 - Stranding (fat, soft tissue)
 - Homogeneous (fat)
 - Mesentery
 - Stranding (fibrofatty change ["creeping fat"])
 - Lymphadenopathy
- Narrowing

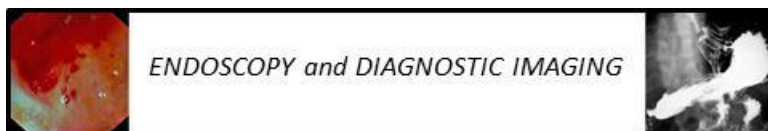
Focal

- Non-specific ("idiopathic") ulcerations
 - Single or multiple ulcers
 - Ulcerative area sharply demarcated from normal area ("isolated" small bowel ulcers)
 - Focal narrowing
 - Diaphragm – like strictures

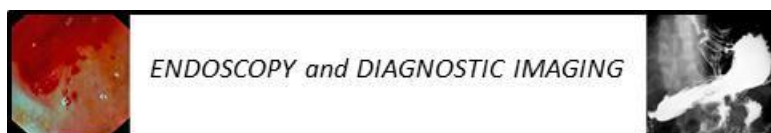
Distinguishing diagnosis: isolated small bowel ulcers

- Nonspecific (idiopathic)
- Infection
 - TB
- Immune
 - Behcet syndrome
 - Celiac disease
- Ischemia
- Heterotropic gastric mucosa
- Trauma
- Drugs
 - Arsenic

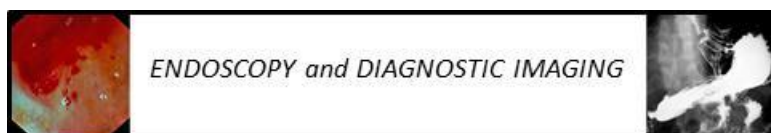
- Intestinal Mycobacterial Tuberculosis (TB)
 - Often with a normal chest X-ray
 - Distal ileum / cecum
 - Narrowing
 - Ulcers

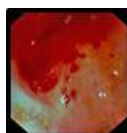


- Segmental
- Mass
- Thickening of wall (separation of folds)
- Fistulae
- Ileocecal valve may be open (“incompetent”)
- Peritonitis
 - Mesenteric
 - Stranding
 - Adenopathy
 - Upper abdomen
 - Low density in centre of nodes
 - Ascites
- Graft-versus-host Disease (GVHD)
 - Thick mucosal folds
 - Wall thickening
 - “ribbon-like” appearance (atrophic, featureless loops of bowel)
 - Stomach, small bowel, colon (skin, liver, GI tract)
 - When GVHD caused by bone marrow transplantation
 - Several days of barium coating of bowel affected by GVHD
- Non rotation of small bowel – position in abdominal cavity:
 - Non rotation
 - All small bowel on right-side of colon
 - All colon of left-sided of colon
 - Incomplete
 - Position in abdominal cavity
 - Small bowel normal
 - Cecum high right side, epigastrium, or left side of abdomen
 - Incomplete mesenteric attachment → mobile cecum
- Multiple Small Bowel Diverticulosis
 - Multiple
 - Large
 - Sac-like out - pouching
- Meckel Diverticulum
 - RLQ, distal small bowel (in distal 3 feet of small bowel)
 - Sac-like out pouching
 - May be associated with
 - Heterotropic gastric mucosa (in 2/3)
 - Calcified enterolitis
 - Obstruction of small bowel
 - Perforation
 - Inversion filling defect in lumen



- Radionucleotide scan technetium pertechnetate secreted by gastric mucosa
 - Meckel diverticulum (heterotopic gastric mucosa in 2/3)
 - Barrett esophagus
 - Duplication cysts
- Normal tissue uptake / secretion
 - Salivary glands
 - Stomach
 - Urinary tract (some isotopic tracer is secreted by kidneys)
- CT Meckel diverticulum diverticulitis: CT signs of inflammation
- Wall thickening
- Mesenteric stranding (of soft tissue)





ENDOSCOPY and DIAGNOSTIC IMAGING

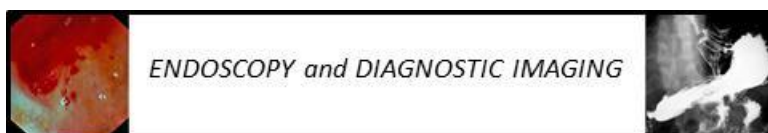


SMALL INTESTINE DIAGNOSTIC IMAGING

CLINICAL SKILLS

Self-assessment

**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**



Case 1

Patient presents with gas, bloating, and diarrhea.

Case 2

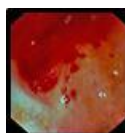
Patient presents with weight loss and chronic diarrhea.

Case 3

Patient presents with abdominal pain and vomiting 3 months after lap' cholecystectomy.

Case 4

25 year old woman presents complaining of intermittent RUQ pain.

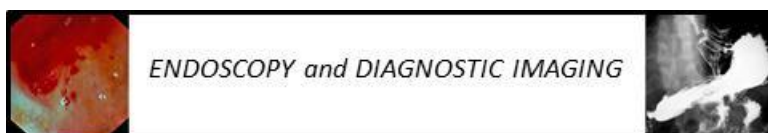


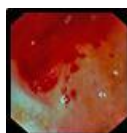
Case 5

69 year old woman presents with one year history of Crohn disease, abdominal pain and weight loss.

Small Bowel Diagnostic Imaging Answers

1. Small bowel follow through; jejunal and ileal diverticulosis
2. Small bowel follow through; dilation fold thickening segmentation (flocculation)
3. Small bowel obstruction, air in biliary tree (gallstone ileus)
4. Duodenal diverticulum containing food particles
5. Narrowing of neo-terminal ileum, fistula.





ENDOSCOPY and DIAGNOSTIC IMAGING



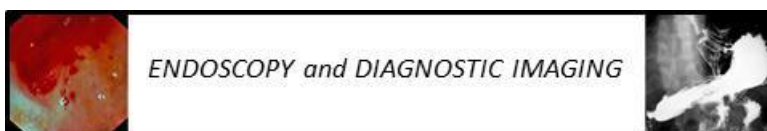
SMALL INTESTINE ENDOSCOPIC IMAGING

CLINICAL SKILLS

Self-assessment

**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**

*Provided through the courtesy of Dr. Edgar Jaramillo, Center of
Gastrointestinal Disease, Ersta Hospital, Stockholm, Sweden*



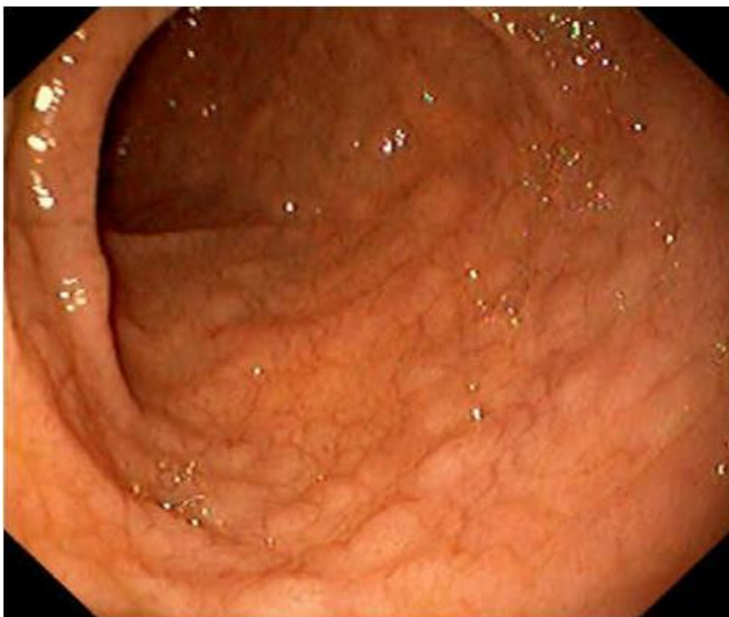
Describe the following small bowel endoscopy photographs, give the differential diagnosis, and state the most likely endoscopic diagnosis.

Case 1



Dyspeptic 60 year old man, proven celiac disease, non-compliant to gluten free diet.

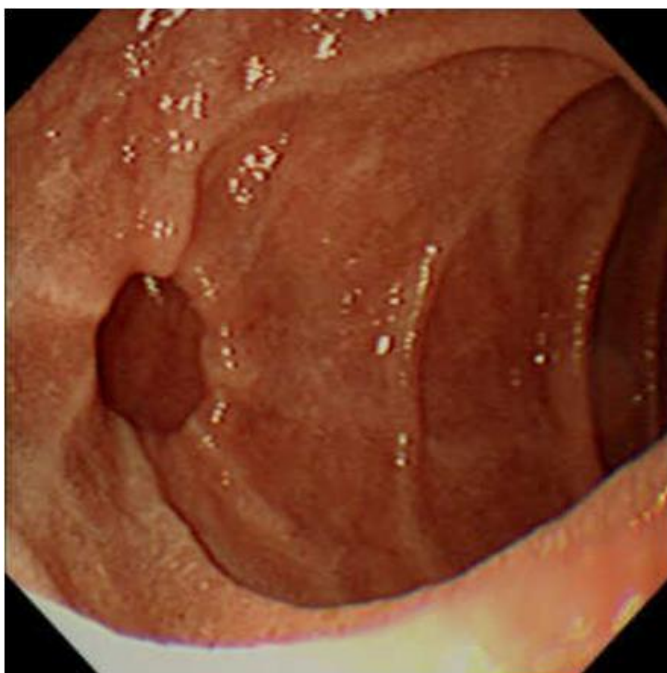
Case 2



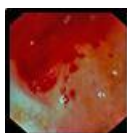
This endoscopy was performed in the daughter of the above patient.

Case 3

Dyspepsia in a 28 year old man on maintenance azathioprine for Crohn's disease of terminal ileum.

Case 4

An incidental finding on endoscopy of the above patient's younger brother who worries.

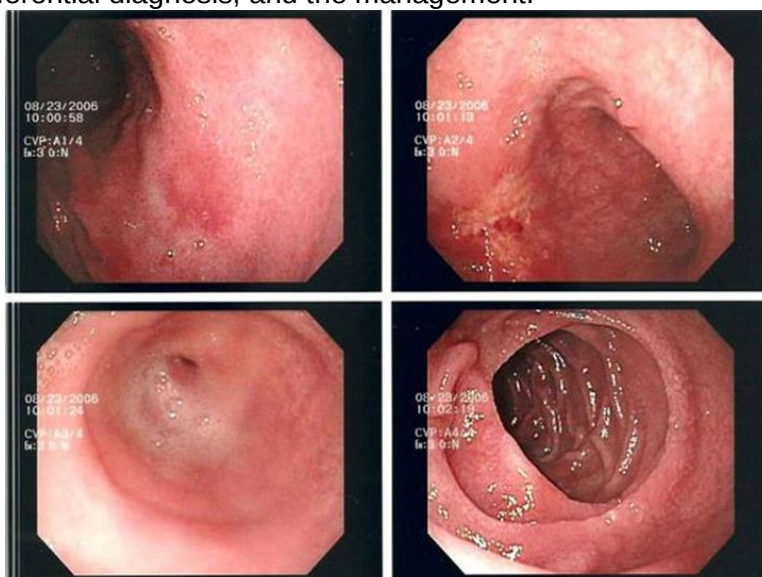


Case 5

An 18 year old with chronic abdominal pain, without alarm symptoms

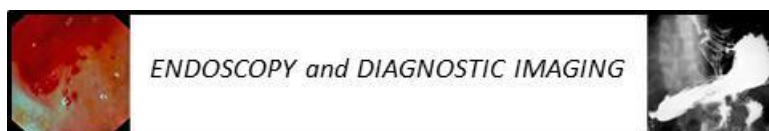
Case 6

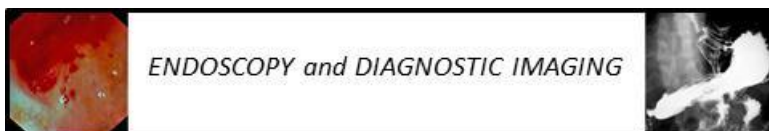
A 75 year old man was referred because of having dermatitis herpetiformis (DH) and diarrhea. Biopsy showed celiac disease. He does well on a gluten-free diet, the diarrhea resolves, but 2 years later begins to lose weight and the diarrhea reoccurs. Please give the endoscopic findings, the differential diagnosis, and the management.



Small Bowel Endoscopy Answers

1. Duodenal carcinoma
2. Celiac disease
3. Crohn disease of small bowel
4. Diverticula of small bowel
5. Ileal lymphoid hyperplasia
6. Scalloping, mosaic pattern, gastritis, sessile polyp, possible gastric lymphoma





PANCREAS

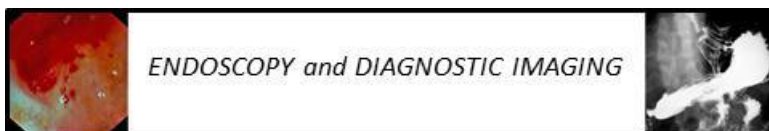
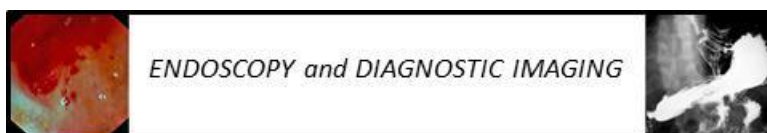


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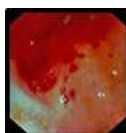
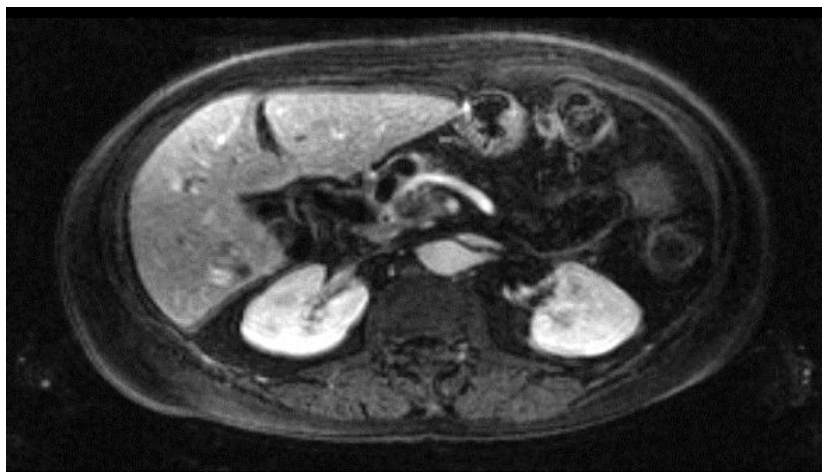
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PANCREAS

“Sharpening Knowledge to Enhance Clinical Skills”

- The etiologic factors for chronic (recurrent) pancreatitis
 - Chronic calcifying variety
 - Chronic ethanol ingestion (>80 g/d)
 - Tropical pancreatitis
 - Hereditary pancreatitis
 - Hyperparathyroidism
 - Chronic obstructive variety
 - Papillary stenosis ± biliary lithiasis
 - Intraductal protein plugging ± calcification
 - Fibrotic, traumatic or malignant obstruction of Wirsung duct
 - Idiopathic variety
 - The causes of inadequate enzyme replacement in the person with pancreatic exocrine insufficiency:
 - Inadequate quantities of enzymes, especially lipase
 - Incorrect timing of administration
 - Inactivation of enzymes by acidic gastric environment
 - Digestion of enzymes by co-administered proteolytic enzymes
 - Incomplete dissolution of enzymes and difficulty in achieving adequate mixing with chyme
 - De-synchronized gastric emptying because of size of microspheres

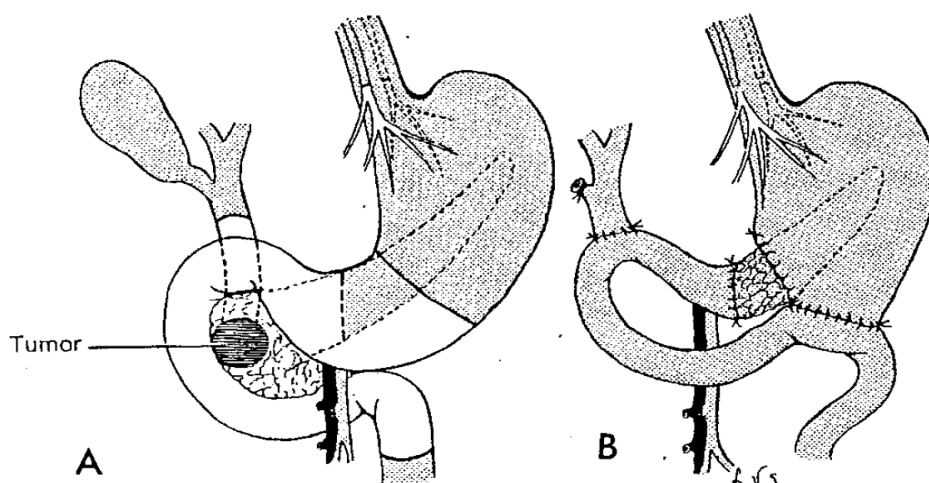


ENDOSCOPY and DIAGNOSTIC IMAGING



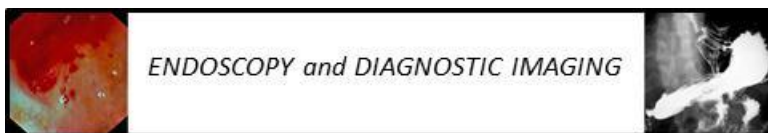
- Advantages of MRCP
 - Non-invasive
 - Parenchymal/anatomy
 - No radiation
 - Fast
 - Inexpensive
 - Easy clinicians (MIP)

Practice Points: Whipple procedure for pancreatic cancer



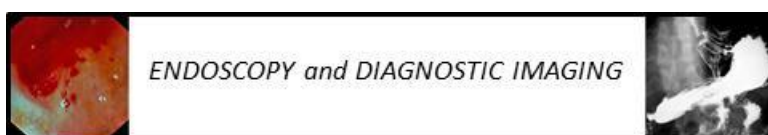
PANCREATIC NEUROENDOCRINE TUMORS

- Gastrinoma
 - 1 per year/ 10^6 population
 - Malignant ~66%
 - 20% association with MEN I
 - 50% of sporadic and > 70% of hereditary gastrinomas are in the duodenum
 - Resection of all sporadic gastrinomas and in MEN ii if >2.5 cm
- Insulinoma
 - 1 per year/ 10^6 population
 - Benign in ~90%
 - Solitary in 95%
 - < 2 cm in 85-90%
 - 4% are MEN I
 - In MEN I patients insulinomas are multiple in 90%
 - Encleation if solitary; pancreatectomy if multiple



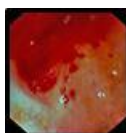
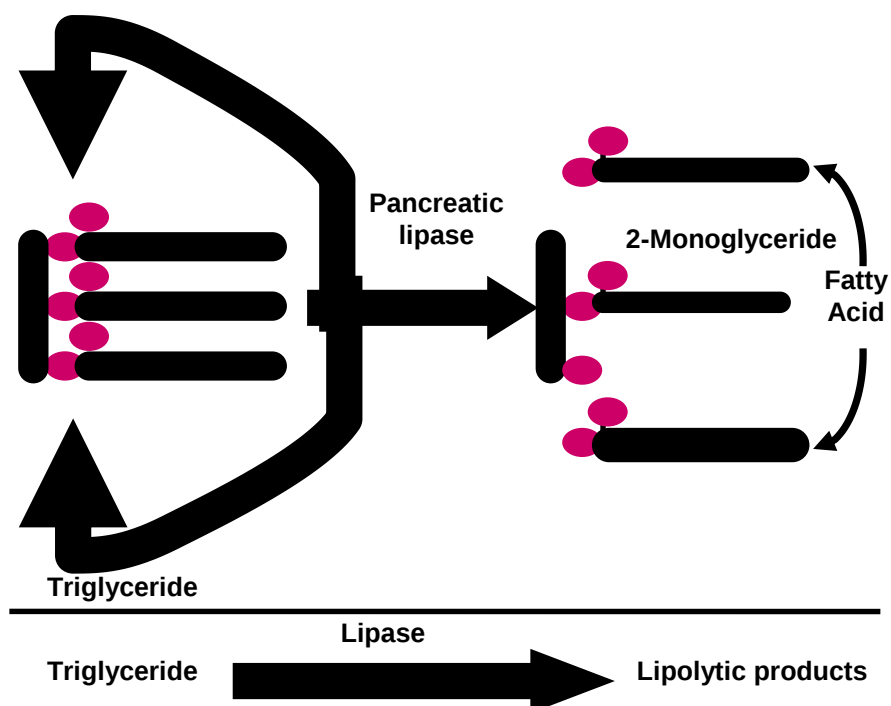
- Non-functional pancreatic neuroendocrine tumors
 - Majority are malignant (>50%)
 - Mostly in pancreas head and often large
 - Have worse survival compared to functioning pancreatic neuroendocrine tumors
 - Resection of all sporadic tumours or if > 2-3 cm in VHL
- Pancreatic Neuroendocrine Tumors in VHL
 - Occur in 10-15% of patients
 - Frequently multiple (>30%)
 - Tumors > 3 cm are aggressive (metastases)
 - Resect lesion if >3 cm in body/tail and if >2 cm in pancreas head
 - Tumours <1 cm require yearly follow-up by CT or MRI from an early age
- Local and Systemic Therapy
- Local
 - Liver resection
 - Chemoembolization
 - Radiofrequency ablation
- Systemic
 - Somatostatin analogues
 - Somatostatin receptor radionuclide therapy
 - MIBG radionuclide therapy
 - Chemotherapy, especially for poorly differentiated tumours
- A classification of cystic lesions of the pancreas
 - Congenital true cysts
 - Inflammatory
 - Angiomatous cysts
 - Cystic neoplasms
 - Acquired cysts
 - Misdiagnosed non-pancreatic lesions
 - Metastases, with cystic component

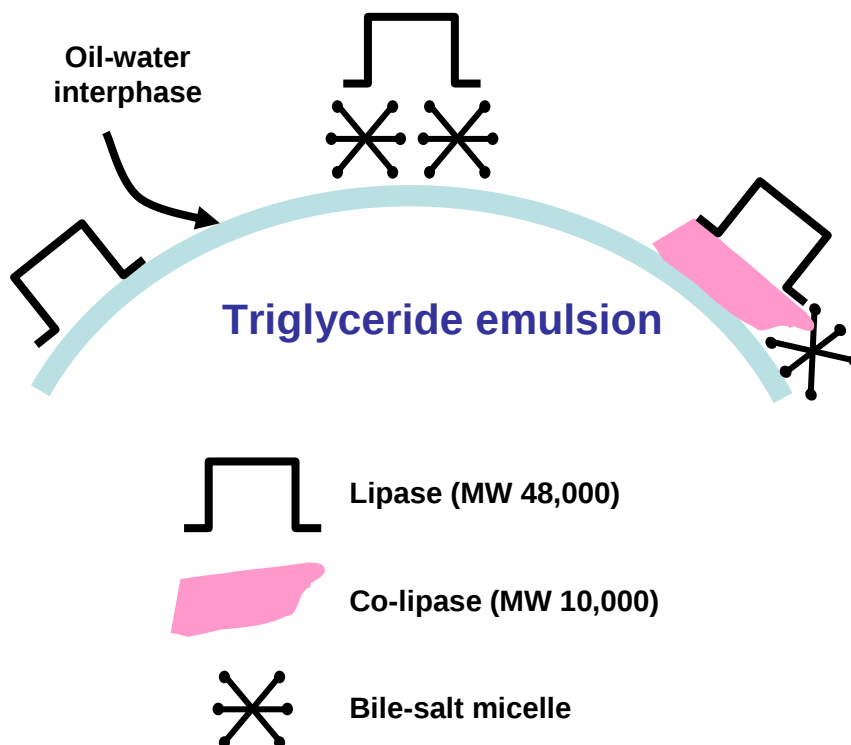
Permission from: Degen L, et al., Best Practice & Research Clinical Gastroenterology, 2008.



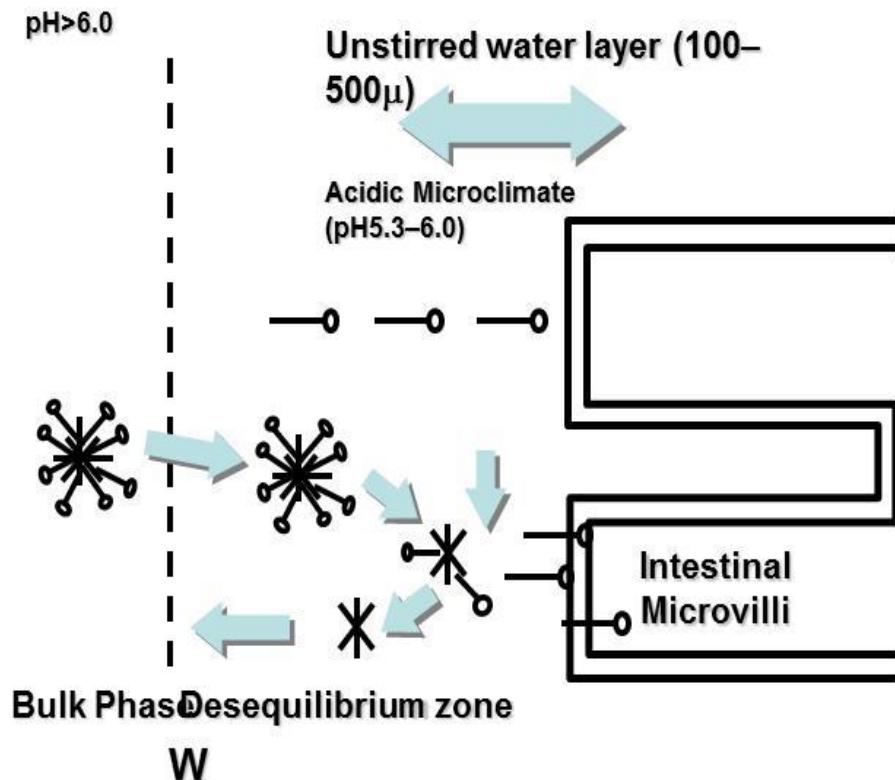
PANCREATIC ENZYME THERAPY

- Positional specificity of pancreatic lipase: Partial Hydrolysis

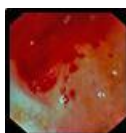




- Human Pancreatic Lipase I
 - Interfacial enzyme, active in the triacylglycerol oil-water interface
 - Inactivated in oil-water interface by hydrophobic denaturation
 - Dependent on clean interface for its lipolytic activity
 - Hydrophobic proteins and phospholipids inhibit lipase by competition for interface
 - Inhibited by bile salts (above CMC); bile salts clean lipase substrate interface of surface-active compounds and physically separate lipase from substrate
- Human Pancreatic Lipase II
 - Colipase binds to lipase in the presence of bile salts; lipase/colipase plus lipolytic products induce conformational change of lipase, opening up hydrophobic binding sites for further substrate
 - Lipase is specific for the primary esterbond of the substrate
 - Lipase is rapidly and irreversibly inactivated at pH <4.0



- Pancreatic Exocrine Function
 - Normal post-prandial pancreatic secretion is $\pm 70\%$ of maximal secretory capacity or 4–5 times the basal rate
 - Post-prandial secretion lasts for about 4 hours
 - Total intraduodenal lipase output varies from 300,000 to 500,000 U/meal
 - Minimum pancreatic function of 10% of normal is necessary for adequate lipid digestion, corresponding to $\pm 30,000$ –50,000 U lipase in the duodenum
 - Amount of lipase, to be added to meals, varies from 30,000–90,000 U depending upon degree in insufficiency and degree of gastric/duodenal denaturation
- Pancreatic Exocrine Insufficiency: Lipid Maldigestion
 - Steatorrhea (mild: 7–10 g/d; moderate: 10–20 g/d; severe: >20 g/d)
 - Impaired CCK release
 - Impaired GIP release
 - Sluggish gallbladder emptying
 - Malabsorption of lipid-soluble vitamins
 - Bile salt precipitation due to duodenal hyperacidity
 - Interaction between calcium and glycine-conjugated bile salts

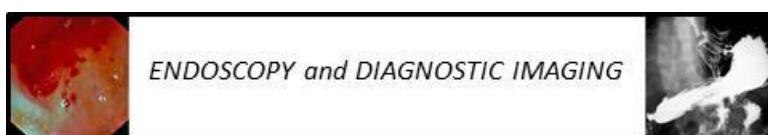


- Increased fecal loss of bile salts
- Increased fecal loss of cholesterol
- Pancreatic Enzyme Therapy: Indications
 - Exocrine pancreatic insufficiency (chronic pancreatitis, pancreatic resection, pancreatic cancer, pancreatic duct occlusion, cystic fibrosis)
 - any moderate / severe steatorrhea
 - any steatorrhea with weight loss
 - chronic / watery diarrhea
 - dyspeptic symptoms
 - Unrelenting pain in chronic pancreatitis (inhibition of pancreatic secretory drive by negative feedback) (non-enteric coated preparations)
- Pancreatic Enzyme Preparations: Enteric Coated Preparations
- Enteric-coated tablet / capsule (dissolving at pH >5)
 - prolonged gastric retention causing de-synchronization
 - failed or delayed dissolution when duodenal pH is low (lack of bicarbonate)
- Enteric-coated microspheres (dissolving at pH >5)
 - premature gastric dissolution when pH >5 during early phase of meal
 - delayed gastric emptying of particles >1.4 mm
 - failed or delayed dissolution when duodenal pH is low

Useful background: Microsphere pancreatic enzyme preparations

	Lipase	Amylase	Protease	Sphere	Diameter
Creon	8,000	9,000	450	1.4	1.2-1.7
Pancreas	5,000	2,900	330	2.0	1.7-2.2
Panzytrat	25,000	22,500	1,250	2.0	
Creon forte	25,000	18,000	1,000	1.4	1.2-1.8

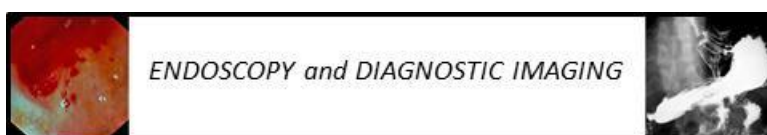
- microspheres larger than 1.4 mm empty more slowly than solid phase of the meal
- release of enzymes from microspheres is slow, depending upon pH and ionic strength of medium



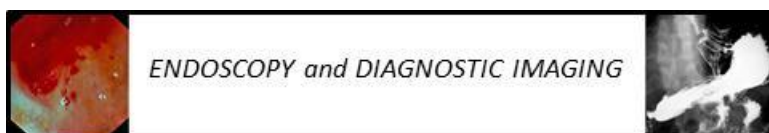
- Pancreatic Exocrine Insufficiency: Dietary Recommendations
- Abstinence from alcohol
- Limitation of fat content of food (<60 g/d) (unpalatable; risk of deficit of essential fatty acids e.g. linoleic acid)
- Frequent small meals
- Reduction in fiber content (fiber inhibits pancreatic enzymes)
- Medium chain triglycerides (C6-C12) (80–120 g/d) in case of insufficiently corrected steatorrhea and weight loss

ACUTE PANCREATITIS

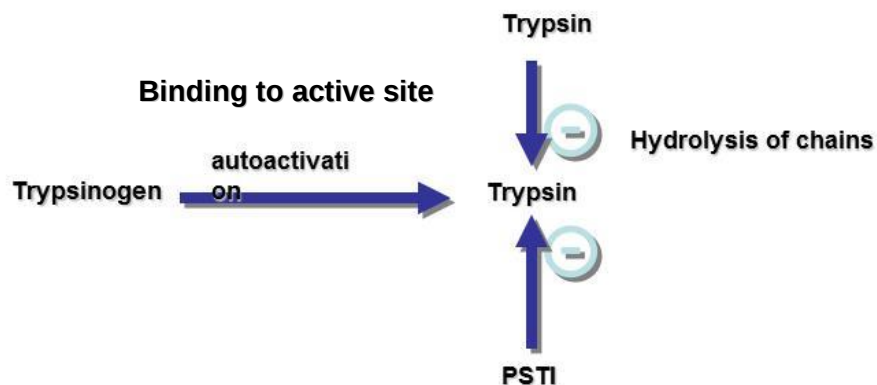
- The major causes of acute pancreatitis
 - Gall stones
 - Alcohol
 - Anatomical (devised pancreas)
 - Drug induced
 - ERCP
 - Trauma (including post surgical)
 - Metabolic (hyperlipidemia, hypercalcemia)
 - Periampullary and pancreatic tumors
 - Miscellaneous (viral, parasites, scorpion bite)
- The local and systemic complications of acute pancreatitis
- Local
 - Sterile necrosis
 - Infected necrosis
 - Abscess
 - Pseudocyst
 - Gastrointestinal Bleeding
- Pancreatitis-related
 - Splenic artery rupture or splenic artery pseudoaneurysm rupture
 - Splenic vein rupture
 - Portal vein rupture
 - Splenic/portal vein thrombosis leading to gastroesophageal varices with rupture
 - Pseudocyst or abscess hemorrhage
 - Postnecrosectomy bleeding
- Non-pancreatitis-related
 - Mallory-Weiss tear
 - Alcoholic gastropathy
 - Stress-related mucosal gastropathy



- Splenic injury
 - Infarction
 - Rupture
 - Hematoma
 - Fistulization to or obstruction of small or large bowel
 - Right-sided hydronephrosis
- Systemic
 - Head and Neck
 - Retinopathy
 - Psychosis
 - CVS
 - Shock (circulatory failure)
 - Lung
 - Respiratory failure
 - Kidney
 - Renal failure
 - Metabolic
 - Systemic (systemic cytokine response, “cytokine” storm)
 - Hyperglycemia
 - Hypocalcemia
 - Hypomagnesemia
 - Hypoglycemia
 - Subcutaneous nodules due to fat necrosis
 - Blood
 - Disseminated intravascular coagulation
 - Miscellaneous
 - Malnutrition
 - Death:
 - Mortality rate - Fairly static at just under 10% despite improved intensive care, diagnostic capabilities, and therapeutic interventions
 - Mild Pancreatitis (80%)→ Morality 1-2%
 - Severe Pancreatitis (20%)
 - Sterile necrosis→ mortality 10%
 - Infected necrosis→ mortality 30%
- ERCP method related
 - Difficult cannulation
 - Pancreatic duct injection
 - Pancreatic sphincterotomy
 - Precut sphincterotomy (by endoscopists of mixed experience)
 - Balloon dilation of biliary sphincter
 - Acinarization (possible)
 - Absent common bile duct stone (possible)

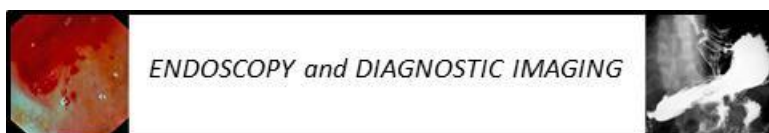


- The mechanisms which prevent inadvertent activation of trypsin in the pancreas (autodigestion)
- Separation of zymogen granules and lysosomes within the acinar cell
- Trypsin inhibitors (spink) exist within the acinar cells and the pancreatic duct
- The digestive enzymes are secreted as precursors
- Activation of trypsin actually occurs OUTSIDE the pancreas by duodenally secreted enterokinases (trypsinogen activated kinase)
- Theory I: Role of Cathepsin B
 - Lysosomal hydrolase cathepsin B localises to compartment where trypsinogen is activated
 - Cathepsin B inhibition ameliorates experimental pancreatitis
- Theory II: Trypsinogen Autoactivation
 - In the normal pancreas small amounts of trypsinogen are constantly activated
 - This process is kept in check by Trypsin itself and PSTI



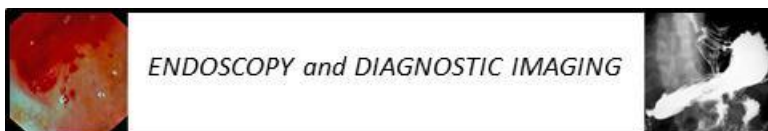
- R122H and PSTI mutations are associated with hereditary pancreatitis
- Mutations are however frequent in general population
- Mutations lower the threshold for acute pancreatitis

****Pancreatitis is caused by a combination of environmental and genetic factors; the primary pathophysiological event is unknown**

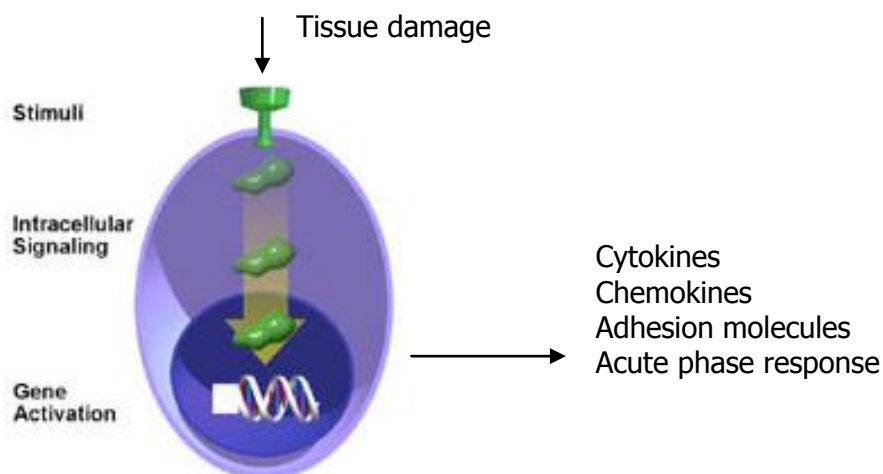


- Lines of evidence for role in pancreatitis
 - NF kappa B activation results in pancreatitis (adenoviral transfer)
 - NF kappa B is activated during AP and highest in areas with most extensive damage
 - Inhibition of NF kappa B ameliorates AP
- Pro-inflammatory cytokines: cytokine cascade: Important pro-inflammatory soluble mediators

TNF-alfa	Early biphasic response
IL1-beta	IL1 receptor KO mice / ICE inhibition protected
IL-6	Marker of severity
PAF	Lipid mediator
	Failed clinical study with PAF inhibitor
- Chemokines
- Platelet activating factor
- Neutrophil influx
- The cellular mechanism of acute pancreatitis:
- Timely course of events
 - Intracellular events: zymogen activation
 - Early local reaction and inflammation
 - Chemokines and proinflammatory cytokines
 - Pancreatic necrosis
 - Systemic inflammatory reaction
 - Distant organ damage
- Inflammatory response
 - Nf kappa B activation
 - Cytokines produced by macrophages and acinar cells
 - Chemokines
 - Platelet activating factor
 - Neutrophil influx



Useful background: Nuclear Factor Kappa B



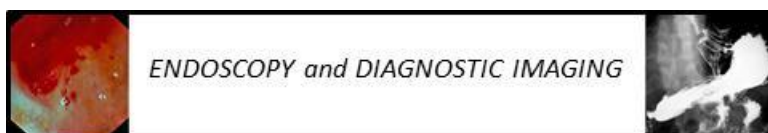
➤ The method of stratification of the severity of acute pancreatitis.

➤ Ranson score (partly on admission, partly during 48 hrs)
 ➤ designed for alcohol etiology
 ➤ less validated

➤ Modified Glasgow score (during 48 hrs)
 Glasgow variant: utilizing AST in preference for age
 ≥ 3 positive criteria = severe acute pancreatitis

Age	> 55 years
Arterial pO ₂	< 8 kPa (< 60 mmHg)
Albumin	< 32 g/L
Calcium	< 2.0 mmol/L
White cell count	> 15 x 10 ⁹ /L
LDH	> 600 IU/L
Glucose	> 10 mmol/L (in absence of DM)
Urea	> 16 mmol/L

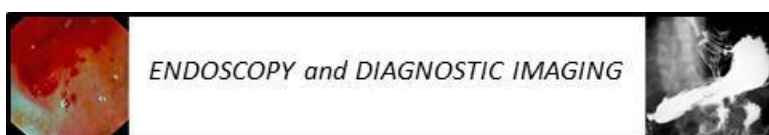
➤ APACHE II score
 ≥ 8 points excludes many that will develop complications
 ≥ 6 points: sensitivity 95%; PPV 50%



- Balthazar score (predictor of subsequent infected necrosis)
Severity Assessment by CT-scan: Balthazar Classification
Balthazar Score:
 - A = normal
 - B = enlarged pancreas
 - C = peripancreatic infiltration
 - D = enlarged pancreas with one fluid collection
 - E = enlarged pancreas with more than two fluid collections
- C-reactive protein (> 120 mg/l, max response at 48 hours)
- Prognostic value of early CT-scan
- Predictive of abscess:
 - non-visualisation of splenic vein
 - collections in right pararenal posterior space
 - heterogenous extrapancreatic collections
- Predictive of death:
 - non-enhancement of the neck of the pancreas
 - extrapancreatic collections in the left or right posterior pararenal spaces
- Diagnosis Necrosis or infected Necrosis?
 - Contrast CT scan
 - only in severe acute pancreatitis
 - no contrast-enhancement of necrotic areas
 - CT- or US-guided fine needle aspiration (FNA)
 - 10% false negative results
 - repeat if no clinical improvement

Practice Pointers: Performance characteristics of Prognostic Scores

	Sensitivity	Specificity	PPV	NPV
Ranson	70%	67%	67%	87%
Glasgow	55%	91%	53%	90%
APACHE II	63%	71%	56%	92%
CRP (48 hrs)	80%	76%	66%	90%
Ranson + CRP	80%	80%		
Glasgow + CRP	80%	87%		
APACHE + CRP	73%	83%		



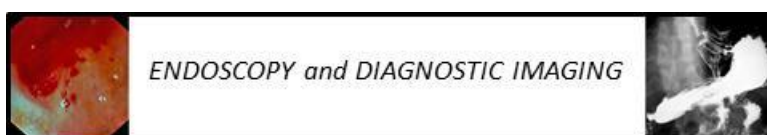
- The complications of acute pancreatitis
 - Septic shock
 - Hemorrhage→pseudoaneurysm splenic artery
 - Colonic necrosis
 - Small bowel fistula→thrombosis superior mesenteric artery/vein
 - Duodenal/pancreatic fistula
 - Duodenal obstruction
 - Pseudocyst
 - Pancreatic abscess
- The causes of an elevated serum amylase/lipase

GI causes	Non-GI causes
➤ Appendix ○ Appendicitis ➤ Small Bowel ○ Small bowel obstruction ○ Intestinal ischemia ○ Bowel perforation ○ Sprue ➤ Gallbladder ○ Cholecystitis ➤ Salivary Gland ○ Salivary gland disease, e.g. mumps ➤ Stomach ○ PUD (penetration) ➤ Pancreas ○ Pancreatic cancer	➤ GU ○ Tubo-ovarian disease, e.g. fallopian tube (salpingitis), ectopic pregnancy ➤ Metabolic ○ Diabetic ketoacidosis ○ IgA deficiency ➤ Infection ○ HIV infection ➤ Nutritional ○ Anorexia ○ Bulimia

Adapted from: Vissers RJ, et al. *J Emerg Med* 1999;17(6):1027-37.

Practice Pointers: Classification of drugs associated with induction of acute pancreatitis

- Class I: implicated in > 20 reports, at least one documented case following reexposure
 - Didanosine
 - Asparaginase
 - Azathioprine

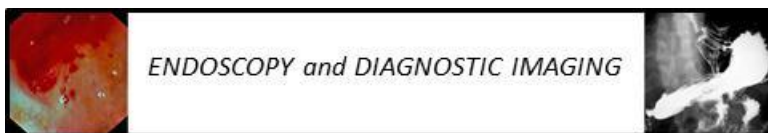


- Valproic acid
 - Pentavalent antimonials
 - Pentamidine
 - Mercaptopurine
 - Mesalamine
 - Oestrogen preparations
 - Opiates
 - Tetracycline
 - Cytarabine
 - Steroids
 - Trimethoprim/sulfamethoxazole
 - Sulfasalazine
 - Furosemide
 - Sulindac
- Class II: implicated in > 10 reports
- Rifampicin
 - Lamivudine
 - Octreotide
 - Carbamazepine
 - Acetaminophen
 - Phenformin
 - Interferon Alfa-2b
 - Enalapril
 - Hydrochlorothiazide
 - Cisplatin
 - Erythromycin
 - Cyclopenthiazide

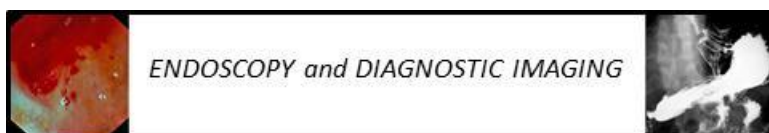
Printed with permission: Keller J, et al. *Best Pract Res Clin Gastroenterol* 2007;21(3):519-33.

Diagnostic imaging

- Inflammatory disease
- Acute pancreatitis
- Diffuse
 - Focal
 - Necrotizing
 - Complications
 - Pseudocysts
 - Abscesses
 - Pseudoaneurysms
 - Splenic / portal vein thrombosis
 - Hemorrhage



- Chronic pancreatitis
- Familial pancreatitis
 - Familial
 - Hereditary
- Autoimmune pancreatitis
- Acute pancreatitis
- Contrast-enhanced CT
- Staging (bathazar)
 - Normal
 - Focal or diffuse enlargement
 - Intrinsic pancreatic abnormality, and peripancreatic inflammation
 - Phlegmon, or fluid collection
 - Two or morw phlegmonous collection, or peripancreatic air
- Focal pancreatitis (20%, B)
 - Head
 - Mild disease
 - Cholelithiasis
- Necrosis (E)
 - Loss of perfusion
 - Complications
 - Infection abscess
 - Pseudoaneurysm
 - Splenic vein (portal vein thrombosis)
 - Biliary obstruction
 - Hemorrhagic pancreatitis
- Pseudocyst
 - Peripancreatic fluid collection
 - Lasts > 6 weeks
 - Thick fibrous wall
 - Contains distinct fat
 - Blurring (loss) of distinct tissue planes between mass and the retroperitoneal fat and peripancreatic tissue stranding
 - Thickening / stranding of soft tissue
 - Peripancreatic fluid collection
 - Communicates with pancreatic duct
- Ultrasound
 - Enlargement
 - Hypoechogenic



- Peripancreatic fluid
- Possible choledocholithiasis

* ultrasound is not of use to differentiate between

- Necrotic vs. non-necrotic pancreatitis (CT of use)
- Is of use to distinguish pseudocyst containing blood or infected fluid (CT shows homogeneous fluid attenuation, so not of use)

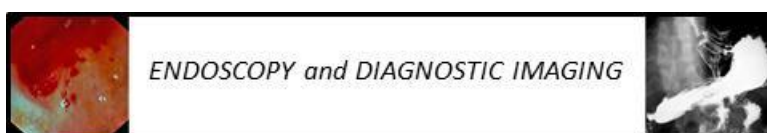
➤ Upper GI barium study

- Duodenal
 - Loop – enlarged
 - Lumen – narrowed
 - Folds – thickened

CHRONIC PANCREATITIS

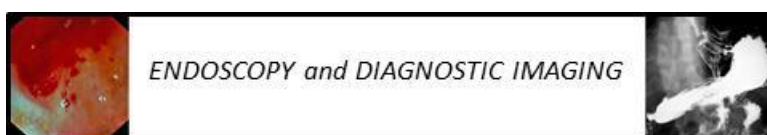
Practice Pointers: The theories of the pathogenesis of chronic pancreatitis

- The Necrosis-Fibrosis Sequence Hypothesis¹
 - Chronic pancreatitis is the result of repeated episodes of acute pancreatitis
 - Supported by:
 - pathological studies
 - long-term clinicomorphological studies²
 - discovery of cationic trypsinogen mutation
- Pathophysiological Mechanisms
 - Tight link between injury, chronic inflammation and fibrosis
 - Pancreatic fibrosis requires differentiation and stimulation of pancreatic stellate cells
 - The primary stimulating agent of pancreatic stellate cells is TGF- β
 - TGF- β originates from monocytes and resident macrophages
- Sentinel Acute Pancreatitis Event (SAPE)
 - SAPE: an episode of pancreatitis that is of sufficient severity to attract monocytes, and to cause differentiation and/or proliferation of pancreatic stellate cells
 - Recurrent acinar cell injury causes cytokine and chemokine release from acinar cells which stimulates resident macrophages
 - The macrophages suppress acute inflammation by releasing TGF- β (and other cytokines) which stimulate pancreatic cells to produce collagen and therefore drive fibrosis



Useful background: The types and causes of chronic pancreatitis

- Definition: Disease of multiple etiology leading to morphologic/histologic changes with both functional and clinical sequelae
- Types
 - Chronic calcifying
 - Chronic ethanol ingestion (>80 g/d)
 - Tropical pancreatitis
 - Hereditary pancreatitis
 - Hyperparathyroidism
 - Chronic obstructive
 - Papillary stenosis ± biliary lithiasis
 - Intraductal protein plugging ± calcification
 - Fibrotic, traumatic or malignant obstruction of Wirsung's duct
 - Idiopathic
- Causes
 - Duct obstruction
 - Benign pancreatic duct obstruction
 - Traumatic stricture
 - Stricture after severe acute pancreatitis
 - Duodenal wall cyst
 - Pancreas divisum
 - Malignant pancreatic duct stricture
 - Ampullary or duodenal carcinoma
 - Pancreatic adenocarcinoma
 - Intraductal papillary mucinous neoplasm
 - Hereditary
 - CT gene
 - Autosomal dominant
 - Hereditary pancreatitis (PRSS1 mutations)
 - Autosomal recessive or modifier genes
 - CFTR mutations
 - SPINK1 mutations
 - IgG4 associated
 - Associated with autoimmune diseases
 - Sjögren's syndrome
 - primary biliary cirrhosis
 - primary sclerosing cholangitis
 - Tropical
 - Tropical calcific pancreatitis
 - Fibrocalculous pancreatic diabetes
 - Metabolic
 - Hypercalcemia



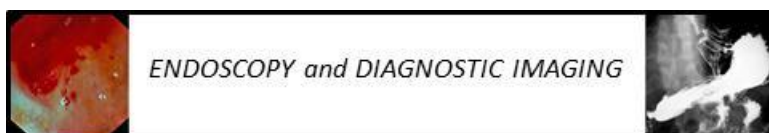
- Hyperlipidemia
- Hypertriglyceridemia
- Lipoprotein lipase deficiency
- Apolipoprotein C-II deficiency
- Diabetes
- Alcohol
- Postnecrotic chronic pancreatitis
- Idiopathic
 - Early-onset
 - Late-onset
- Asymptomatic pancreatic fibrosis
 - Chronic alcoholism
 - Old age
 - Chronic renal failure
 - Diabetes
 - Radiotherapy

Adapted from: Chari ST. *Mayo Clinic Gastroenterology and Hepatology Board Review*; pg 470.; Forsmark CE. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006; pg. 1274.; and Keller J, and Layer P. *Best Practice & Research Clinical Gastroenterology* 2008; 22(1): pg. 106.

Useful background: The tests of exocrine pancreatic functions.

- Direct invasive intubation tests
 - CCK/secretin stimulation
 - Lunch meal
 - ERCP and pancreatic aspiration
- Indirect non-invasive tests
 - Stool fats and nitrogen
 - Stool trypsin and chymotrypsin
 - Breath tests
 - Oral function tests (benitiromide test and pancreolauryl test)
- Blood determinations
 - Trypsinogen
 - Lipase
 - Pancreatic amylase

Adapted from: Pandol SJ. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management* 2006; pg. 1197-1199.



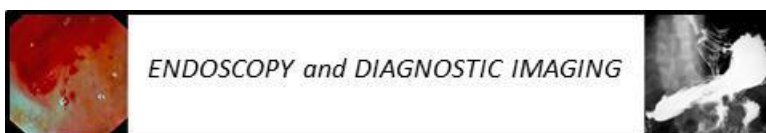
Practice Pointers: Trivia

- Accuracy of detection on abdominal ultrasound: gallstones, > 90%; dilated CBD, 55-91%; CBD stones, 20-75%
- Contrast enhanced CT useful to grade pancreatitis, and to detect necrosis as well as neoplasm; equivalent to gadolinium-enhanced dynamic MRCP (but contrast-enhanced MRCP is superior to contrast enhanced CT to detect CBD stones) (Arvanitakis M, et al. *Gastroenterology* 2005:715-23).
- Microlithiasis occurs in 37-89% of persons with idiopathic acute pancreatitis, and some experts recommend cholecystectomy for associated symptoms
- Definitions
 - Microlithiasis, stones < 3 mm
 - Biliary sludge, a suspension of crystals, mucin, glycoproteins, cellular debris, and proteinaceous material
 - Biliary crystals, crystals of calcium bilirubinate, calcium carbonate, or cholesterol monohydrate; the use of duodenal drainage to assess the presence of biliary crystals has a sensitivity of 65%, and a specificity of 94-100%
- The risk of pancreatitis following ERCP is high in persons with IAP (idiopathic acute pancreatitis) sphincter of Oddi dysfunction (SOD), or a post history of pancreatitis (12.5% risk)

Practice Pointers:

EUS Features/criteria for Chronic Pancreatitis

Ductal Criteria	Parenchymal criteria
Dilated main pancreatic duct (MPD)	Focal areas of reduced echogenicity
Irregularity MPD (strictures, dilations)	Echogenic/hypoechoic foci
Visualization of side branches	Echogenic bands/strands
Increase of echogenicity of MPD wall	Enlarged gland
Intraluminal echo's	Accentuation of lobular architecture
MPD disruption/cyst formation	- Cavities/cysts
	- Shadowing (parenchymal) calcifications



Useful background: Pathology Correlates of EUS Feature

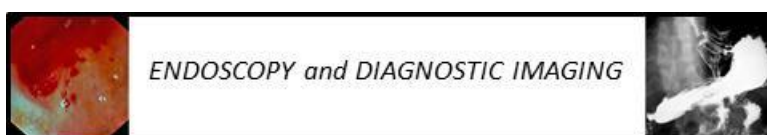
EUS Feature	Pathology correlate
Intraductal echogenic foci	Stones calcifications
Echogenic duct wall	Ductal fibrosis
Side branch ectasia	Periductal fibrosis
Inhomogeneous echo-pattern	Edema
Enhanced echogenic foci	Calcifications
Prominent interlobular septae	Fibrosis
Lobularity	Fibrosis, glandular atrophy

Practice Pointers: Uses of stents in chronic pancreatitis

Pancreatic stones	very helpful as temporary measure
Pancreas Divisum	most helpful in ARP, less helpful in CP
Dominant Stricture	helpful but no controlled studies
Disrupted Duct	clinical success in 60–70%
Pancreatic Fistula	closure in 50–60%
Pancreatic Pseudocyst	resolution in 80–90%, recurrence in 15–20%
Biliary Stricture	clinical improvement in 90–100%
	definitive treatment in 15–30% metal stents in 90%

Useful background: The current approaches to the management of pain in the patient with chronic pancreatitis

- General measures
 - Manage associated/causative factors
 - Cessation of alcohol intake
 - Analgesics
 - Gabapentin
 - SSRIs, TCAs
- Neural interruption
 - Percutaneous or endoscopic (EUS) nerve blocks
 - Surgical (thoracoscopic) splanchnic nerve resection
- Reduction of intrapancreatic pressure
- Suppression of enzyme secretion

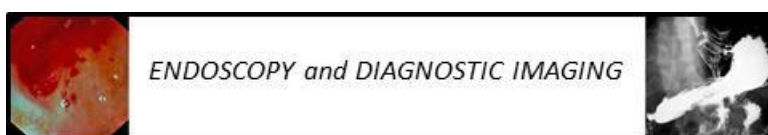


- Anticholinergics, PPI, somatostatin, pancreatic enzyme replacement
- Decompression techniques
 - Sphincterotomy, endoscopic dilation and stenting
 - Stone removal (endoscopic or ESWL)
- Surgical drainage, if pancreatic duct dilated (Peustow)
- Organ resection
 - Partial, complete, with/without pancreatic islet cell transplant

Useful background: The role of endoscopic procedures in the management of acute/chronic pancreatitis

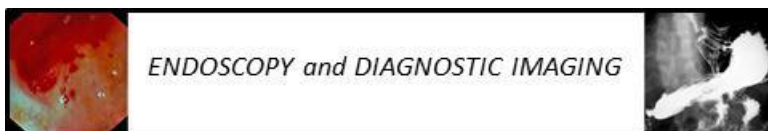
- ERCP
 - Sphincterotomy
 - Dilation and stenting of pancreatic strictures
 - Removal of pancreatic duct stones
 - Pancreatic duct disruption and pseudocyst
 - Biliary strictures from chronic pancreatitis
 - Pancreas divisum
 - Aspirate cyst fluid
- EGD
 - Jejunal tube placement for enteral feeding
- EUS
 - CBD stones
 - Celiac nerve block and neurolysis
- Indication for Treatment of Pancreatic Pseudocyst
 - Pseudoaneurysm formation
 - Fistula (adjacent viscera)
 - Expansion of pseudocyst
 - Abdominal pain
 - Duodenal biliary
 - Abscess formation
 - Pancreatic ascites in peritoneal or pleural cavity
 - Rupture
 - 6 cm, 6 weeks after pancreatitis episode
 - Concern for malignant cystic lesion

Adapted from: Kim HC, et al., Acta Radiol. 2008; Christensen NM et al., Am J Surg.



Diagnostic imaging

- Abdominal plain radiograph
 - Multiple plain radiograph
 - Multiple calcifications
 - Calcifications in pancreatic ducts
- Ultrasound
 - Small, multiple echogenic
 - (white) calculi
 - Posterior shadowing with larger calculi
 - Enlargement of pancreas
 - Hypoechogenic
 - Duct obstruction
 - Dilation
 - Beaded
 - Atrophy
- Contrast – enhanced CT
 - Parenchyma
 - Large, normal, or atrophic (predominant finding)
 - Ducts
 - Dilated
 - Main duct, to ampulla
 - Side duct dilation
 - Differentiation from IPMN
 - Strictures
 - Calcification (50%)
 - Parenchymal fat (replacement of pancreatic tissue with fat arising from duct obstruction from calculi ducts)
 - Pancreatic cancer (2% to 3%)
- ERCP / MRCP
 - Duct
 - Dilation
 - Irregular contour
 - Side branches of ducts
 - Stenosis / clubbing
 - “chain-of-larks” (beading of side branches)
 - Duct lumen –filling defects (calculi)



Diagnostic challenges: dominant changes in chronic pancreatitis vs. IPMN

Chronic pancreatitis

Atrophy

Intraductal pancreatic mucinous neoplasm (IPMN)

Duct dilation

Calculi and pancreatic disease

Chronic pancreatitis

Small, irregular shape stones

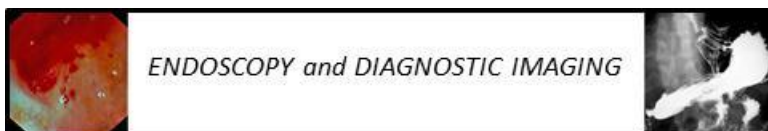
Ducts dilated

Familial pancreatitis, cystic fibrosis

Large stones

Ducts not dilated

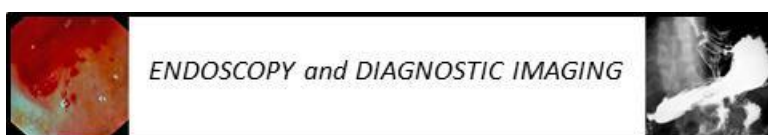
- Familial Pancreatitis
 - Intraductal stones (calculi, calcifications) – large, coarse
 - Pancreatic ducts
 - Dilated
 - Soft tissue
 - Stranding
- Types of familial pancreatitis
- Familial
 - Hyperlipidemia
 - Hyperparathyroidism
 - Cholelithiasis
 - Cystic fibrosis
- Hereditary (autosomal dominant)
- Hemorrhagic pancreatitis
- Unenhanced CT
 - High attenuation in multiple areas
 - Often associated pancreatic necrosis
- Pancreatic Abscess
- Plain film (“abdominal radiograph”)



- In the luminal GI tract
 - Mass effect on
 - Stomach: anterior displacement
 - Colon: inferior
 - Inflammatory changes
 - Thick folds
 - Spasm
 - Narrowing
 - Often the splenic flexure
 - In the pancreas
 - Signs of pancreatitis
 - Distention
 - Proximal and transverse colon
 - Sharp cut-off distention at splenic flexure (colonic “cut off” sign)
- CT scan
 - Peripancreatic fluid
 - Air in pancreas
 - Pancreatics – colonic fistula
 - Pancreatic abscess
- Contrast – enhanced CT
 - Abnormal fluid collection
 - Air in lesion (20%)
- Barium enema
 - Colon cut off sign pancreatic abscess with inflammatory narrowing of colon
 - Dilation of colon proximal to the splenic flexure

Useful background: The placement of temporary prophylactic pancreatic duct stents is suggested for high risk patients following ERCP. Below are features giving a high and a low risk of post-ERCP pancreatitis.

High	Low
➤ Ampullectomy	➤ Female
➤ Recent biliary sphincterotomy	➤ Young
➤ Sphincter of Oddi dysfunction	➤ Non-dilated bile ducts
➤ Prior episode of post-ERCP pancreatitis	➤ Trainee participation in procedure



Useful background: The pros and cons of pancreatic stents vs a NG drain

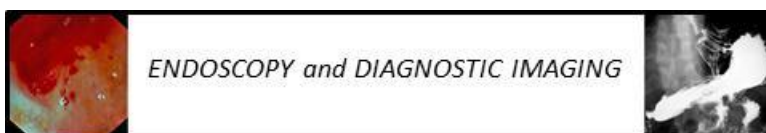
Nasocystic drain	Stent
➤ Flushing and fluoroscopy at any time	➤ Easy, quick, dislocation rare; not disabling, patients stay mobile, feel better
➤ Discomfort; easily dislocated; leads to immobilization of patients, nose-pain	➤ No flushing; control needs endoscopic session
➤ Flushing often futile and tedious, no direct control during flushing	

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AUTOIMMUNE PANCREATITIS

Useful background: The histological and diagnostic imaging features, serology and pancreatic organ involvement, and response to steroid therapy in autoimmune pancreatitis (AIP)

Category	Criteria
➤ Histological features	➤ Diagnostic: ○ Periductal lymphoplasmacytic infiltrate with obliterative phlebitis (LPSP) in pancreatic tissue ○ High (>10 cells/hpf) IgG4 positive cells in the pancreas
➤ Diagnostic imaging	○ Lymphoplasmacytic infiltrate with fibrosis in the pancreas
➤ Serology	○ CT/MR: diffusely enlarged gland with delayed enhancement
➤ Other organ involvement	○ ERCP: diffusely irregular, attenuated main pancreatic duct
➤ Steroid therapy	○ Atypical imaging features: pancreatitis, focal pancreatic mass, focal pancreatic duct stricture, pancreatic atrophy
	○ Elevated serum IgG4 level
	○ Persistent distal biliary stricture, parotid/lacrimal gland involvement, mediastinal lymphadenopathy, retroperitoneal fibrosis.
	○ Resolution of pancreatic/extrapancreatic manifestation with steroid therapy.

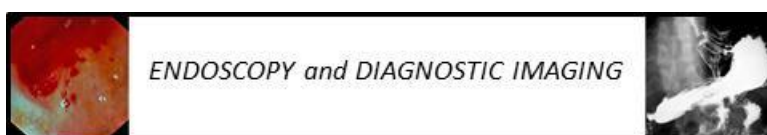


Practice Pointers: Autoimmune pancreatitis (AIP)

- IgG4-associated systemic disease (ISD) (Chari 09)
- Focal, but usually diffuse involvement of pancreas with irregular narrowing of pancreatic duct, swelling of parenchyma, from periductive lymphoplasmacytic infiltration, storiform fibrosis, obliterative phlebitis (infiltrative surrounds venules but not arteriols), and IgG4 positive immunostaining of $\geq$ IgG4 positive cells per HPF
- Type I, lymphoplasmacytic sclerosing pancreatitis, and type II idiopathic duct centric pancreatitis
- ISD may affect pancreas, bile ducts, salivary glands, kidneys, retroperitoneum, and lymph nodes
- More frequently males (80%), over 50 years (80%)
- Pain is not a prominent feature
- CT/MRI shows “sausage-shaped” enlargement of pancreas, peripheral (RIM) enhancement, and delayed enhancement; ERCP shows characteristic diffusely irregular and narrowed pancreatic duct
- Elevated serum IgG4 is 75% sensitive and 93% specific for AIP; IgG4 > 2XULN are highly specific, but $\uparrow$ IgG4 may also be seen in 1.5% of pancreatic cancers
- Consistent response to 30-40 mg prednisone, tapering with improvement in serum IgG4 and imaging

Useful background: The diagnostic imaging of autoimmune chronic pancreatitis (AIP) versus alcoholic chronic pancreatitis (ACP)

Finding	AIP	ACP
➤ Duct	○ Narrowing	- Duct dilation
➤ Pseudocyst	○ Rare	- Common
➤ Calcification or stone	○ Rare	- Common
➤ Pancreatic parenchyma	○ Enlargement	- Atrophy



Useful background: Japan pancreas society criteria for the diagnosis of AIP

- Diagnostic criteria: for diagnosis, criterion I must be present together with criterion II and/or III
 - I. Imaging criterion: diffuse narrowing of the main pancreatic duct with irregular wall (more than one third the length of the entire pancreas) and enlargement of the pancreas
 - II. Laboratory criterion: abnormally elevated levels of serum gammaglobulin and/or IgG, or the presence of autoantibodies
 - III. Histopathologic criterion: marked lymphoplasmacytic infiltrate and dense fibrosis

Abbreviations: AIP, autoimmune pancreatitis; IgG, immunoglobulin G

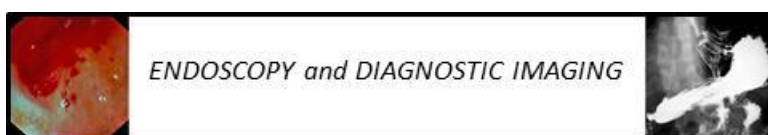
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Useful background: Diagnostic groups of AIP

- Group A: diagnostic pancreatic histology
 - Presence of one or more of the following criteria:
 - Specimen demonstrating the full spectrum of LPSP
 - >10 IgG4 cells/HPF on immunostatin of pancreatic lymphoplasmacytic infiltrate
- Group B: typical imaging and serology
 - Presence of all the following criteria:
 - CT or MRI scan showing diffusely enlarged pancreas with delayed and 'rim' enhancement
 - Pancreatogram showing diffusely irregular pancreatic duct
 - Elevated serum IgG4 levels
- Group C: response to corticosteroids
 - Presence of all the following criteria:
 - Unexplained pancreatic disease after negative workup for other etiologies
 - Elevated serum IgG4 and/or other organ involvement confirmed by presence of abundant IgG4 positive cells
 - Resolution or marked improvement of pancreatic and/or extrapancreatic manifestations with corticosteroid therapy

Abbreviations: AIP, autoimmune pancreatitis; CT, computed tomography; HPF, high power field; IgG, Immunoglobulin G;; LPSP, lymphoplasmacytic sclerosing pancreatitis; MRI, magnetic resonance imaging

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Useful background: The indications for surgery in persons with chronic pancreatitis

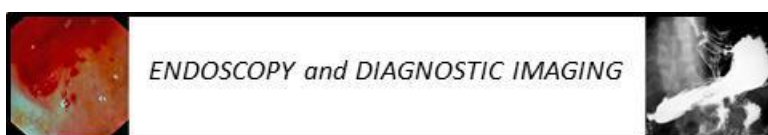
- Intractable pain
- Suspicion of malignancy
- Common bile duct obstruction
- Symptomatic duodenal obstruction
- Symptomatic pseudocysts
- Vascular obstruction
- Pancreatic duct obstruction

Practice Pointers:

- Factors favoring complete removal of pancreatic duct stones
 - Three or fewer stones
 - Stones confined to the head and/or body
 - Stone diameter of <10 mm
 - Absence of impacted stones
 - Absence of a downstream stricture
 - Symptomatic improvement was most evident in patients with chronic relapsing pancreatitis as compared patients with continuous pain

Useful background: Pancreatic pseudocysts

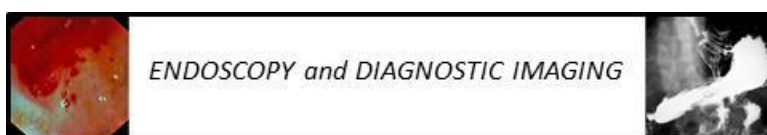
- Definition and Etiology
 - Maturing collection of pancreatic juice encased by reactive granulation tissue occurring in or around the pancreas
 - Acute pancreatitis
 - necrosis of (peri) pancreatic tissue
 - liquefaction with subsequent organization
 - eventual evolution into pseudocyst
 - Chronic pancreatitis
 - following acute exacerbations
 - result from ductal obstruction/leakage
- “To treat or not to treat”
 - Natural history
 - more than 50% of pseudocysts resolve spontaneously
 - size is an important predictor
 - Possible complications
 - hemorrhage
 - perforation
 - infection
 - Treatment recommendations



- wait at least 6 weeks before even considering treatment
 - 6 cm and increasing in size or symptomatic
 - more and more a “wait and see” policy is adopted
- Treatment options
- Surgery
 - complication rate $\pm$ 15%
 - mortality rate <5%
 - postoperative recurrence rate $\pm$ 10%
 - Percutaneous drainage
 - involves prolonged external catheter drainage
 - complication rate $\pm$ 20%
 - mortality rate $\pm$ 5%
 - recurrence rate $\pm$ 7%
 - Endoscopic drainage
 - “Conventional” endoscopic drainage procedure is a relatively “blind” procedure
 - EUS can be used to interrogate the wall and immediate proximity of the cyst
 - intervening vessels
 - measurement of distance between wall and cyst lumen
 - “safe” puncture spot
 - Convex linear array instruments can be used to puncture a cyst under direct EUS guidance

Useful background: The indications for treatment of a person with a pancreatic pseudocyst

- Pseudoaneurysm formation
- Fistula formation into adjacent viscera
- Expansion of the pseudocyst producing abdominal pain
- Expansion of the pseudocyst producing duodenal or biliary obstruction
- Abscess formation.
- Pancreatic ascites (tracking of pancreatic juice into the peritoneal cavity or pleural space)
- Pleural effusion
- Rupture
- >6 cm, 6 weeks after episode of pancreatitis
- Concern for malignant cystic lesion



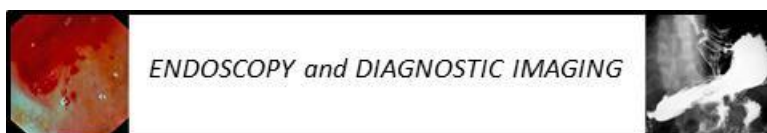
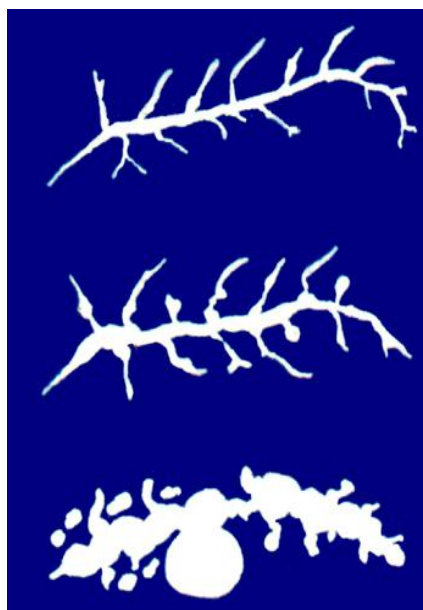
Useful background: The tests to seek a cause of pancreatitis prior to diagnosing the patient as having idiopathic pancreatitis

- Structural (ERCP/MRCP, CT)
 - Pancreas Divisum, chronic pancreatitis, ampullary stenosis, juxta-ampullary diverticulum, or other anatomic abnormalities.
 - ERCP with bile aspiration, centrifugation and examination of pellet for biliary crystals
 - SOD dysfunction (pressure measurement)
- Hereditary
- CFTR gene
 - cationic trypsinogen (CT) gene
 - SPINK gene
 - Test for autoimmune pancreatitis (IgG4 level)
 - Sphincter of Oddi pressure measurement for SOD (sphincter of Oddi dysfunction)

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Practice Pointers: Intraductal Papillary mucinous neoplasms (IPMN)

- Lesions of main or branchial pancreatic ducts, with proliferation of the mucinous epithelium leading to ductal and cystic dilation
- Three types of IPMN, including main, branched or main plus branched (mixed) pancreatic ducts
- 20-30% of IPMNs are multifocal, arising from a field defect in the entire pancreas that can cause multiple primary neoplasms (Brugge 09)
- Range histologically from benign, low grade (LGD), or high grade dysplasia to invasive cancer, with various grades of histology, probably being present with the same specimen
- Mild: Normal or only slightly dilated main pancreatic duct, mild ectasia of side branches. No pseudocyst, no concretions
- Moderate: Dilatation, caliber fluctuations, mild tortuosity main pancreatic duct. Mild cystic dilation, stenosis or obstruction of side



- branches.
- Severe: Beading, stenosis, obstruction, cyst formation, calculi in main pancreatic duct or side branches

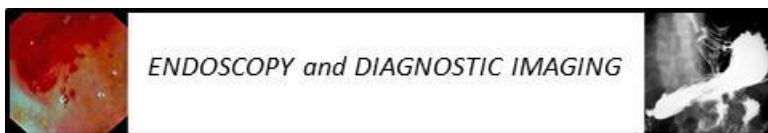
Diagnostic imaging

- Autoimmune Pancreatitis
- Contrast enhanced CT
 - Body enlargement
 - Low attenuation
 - Focal or diffuse
 - Ducts
 - Narrowing

PANCREATIC CANCER

Practice Pointers: Pancreatic Cancer

- A classification of cystic and cystic-appearing lesions of the pancreas
- Congenital true cysts
 - Polycystic disease
 - Von Hippel-Lindau disease
 - Cystic fibrosis
 - Dermoid cysts
- Inflammatory
 - Pseudocysts
 - Abscess
 - Hydatidic cyst
- Angiomatous cysts
- Cystic neoplasms
 - *Mucinous tumors*
 - Mucinous cystadenoma (macrocytic adenoma) and cystadenocarcinoma
 - Intraductal mucin hypersecreting neoplasm; “Mucinous ductal ectasia”
 - *Non-mucinous tumors*
 - Serous cystadenoma (microcystic adenoma)
 - Papillary cystic tumor
 - Cystic cavitation of pancreatic adenocarcinoma or lymphoma



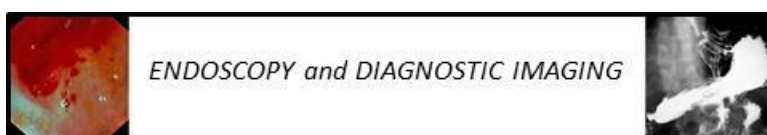
- Acquired cysts
 - Central cavitory necrosis
 - Pseudocyst
 - Parasitic cyst
- Misdiagnosed nonpancreatic lesions
 - Splenic artery aneurysm
 - Choledochal cyst
 - Mesenteric cyst
 - Duodenal duplication cyst or diverticulum
 - Lesser sac biloma
 - Lymphangioma
 - Hypoechoic solid tumor
- Metastases, with cystic component

Practice Pointers: The therapeutic approach (monitor, drain, resect) for cystic lesions in the head, body, and tail of the pancreas

Site	Mucinous	Malignant	Serous	Pseudocyst
Head	Monitor	Resect	Monitor	Drain
Body	Resect	Resect	Monitor	Drain
Tail	Resect	Resect	Resect*	Resect

Useful background: Intraductal papillary mucinous neoplasms (IPMN)

- Lesions of main or branchial pancreatic ducts, with proliferation of the mucinous epithelium leading to ductal and cystic dilation
- Three types of IPMN, including main, branched or main plus branched (mixed) pancreatic ducts
- 20-30% of IPMNs are multifocal, arising from a field defect in the entire pancreas that can cause multiple primary neoplasms (Brugge 09)
- Range histologically from benign, low grade (LGD), or high grade dysplasia to invasive cancer, with various grades of histology, probably being present with the same specimen
- Main branch IPMNs are more likely to become malignant and to grow faster: 63% develop HGD/cancer in 5 years, vs 15% for branched chain IPMNs
- As compared with pancreatic adenocarcinoma, in IPMN there are more frequent molecular changes in SKT 11/LKB1 inactivation and PIK3CA mutation, and less frequent mutations in K-ras and P53 tumor suppressor genes, P16 and DPC4

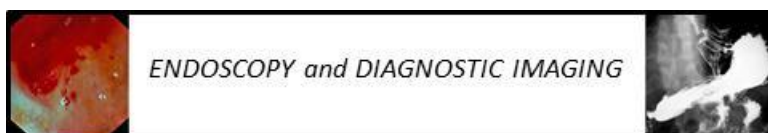


- In IPMN, overexpression of fascin (an actin-bundling protein), methylated PPENK, and human telomerase reverse transcriptase
- Male: female ration 1-2.4, mean age of diagnosis is 65 years; symptoms arise from mucin distending involved pancreatic duct; (may see mucus extruding from ampulla on ERCP)
- Increased serum bilirubin predicts the presence of malignancy
- Grape-like cluster of cysts, localized or diffuse dilation of main pancreatic duct, patulous ampulla of Vater
- Diagnosis: MDCT (multidetactable CT), MRCP, breath-hold MRCP, MRCP with secretin (S-MRCP), CT using pancreatic protocol (detects IPMN in 97% of cases), EUS, ERCP
- ↑ CEA in 80-95%
- PET scanning sensitivity, 57-90%, specificity, 85-97%
- MRCP is superior to CT to demonstrate communication between ducts, and cyst morphology
- Exclude pancreas divisium (MRCP, 100% accurate; CT, sensitivity 90%, specificity, 97%)
- Main duct IPMN or bronchial chain IPMN > 3 cm are more likely to be malignant. Cyst ablation with ethanol or paclitaxel (a chemotherapeutic agent which inhibits the disassembly of microtubules and induces apoptosis with complete resolution of cysts in 79% (234-37) may be reasonable for IPMNs with low risk of malignancy;
 - No symptoms
 - Main duct < 6 mm
 - No mural nodules, thickness or septations
 - < 3 cm size
- After surgical resection, invasive > 40%, non-invasive > 70%; resections recur in a median of 20 months, and 58% of these recurrences involve distal sites

Abbreviations: HGD, high grade dysplasia; IPMN, intraductal papillary mucinous neoplasms; LGD, low grade dysplasia; MDCT, multidetactable CT, S-MRCP, MRCP with secretin

Practice Pointers: Indications for treatment of a person with a pancreatic pseudocyst

- Pseudoaneurysm formation
- Fistula formation into adjacent viscera
- Expansion of the pseudocyst producing abdominal pain

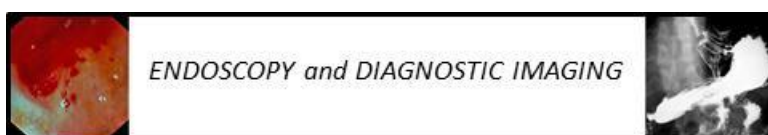


- Expansion of the pseudocyst producing duodenal or biliary obstruction
- Abscess formation.
- Pancreatic ascites (tracking of pancreatic juice into the peritoneal cavity or pleural space)
- Pleural effusion
- Rupture
- >6 cm, 6 weeks after episode of pancreatitis
- Concern for malignant cystic lesion

Useful background: The differences between pancreatic serous cystadenoma, mucinous cystadenoma, IPMT (Intraductal papillary mucinous tumour) and pseudocyst.

	Serous cystadenoma	Mucinous cystadenoma (MCN)	IPMT	Pseudocyst
Clinical				
Sex	Female (2-3:1)	Female (~100%)	Male (3-4:1)	Male
Age	60s	Adenocarcinoma (50s-60s) Carcinoma (60s-70s)	60s	Variable
Ethanol abuse	No association	No association	No association	Yes
Pancreatic history	Yes (uncommon)	Yes (uncommon)	yes (uncommon)	Yes (uncommon)
Malignant potential	No (rare)	Yes	yes	No
Location	Evenly distributed body/tail	Body/tail	head	Head
Imaging studies				
Locularity	Multiple small	multilocular	multilocular	Unilocular
Calcifications	Yes (central sunburst or stellate)	Yes (peripheral, curvilinear)	no	No, unless associated with chronic pancreatitis

Adapted from: Scheiman JM. *AGA Institute Postgraduate Course* 2006: pg. 586.



Useful background: Therapeutic approach for cystic lesion

	Mucinous	Malignant	Serous	Pseudocyst
Head	Monitor	Resect	Monitor	Drain
Body	Resect	Resect	Monitor	Drain
Tail	Resect	Resect	Resect	Resect

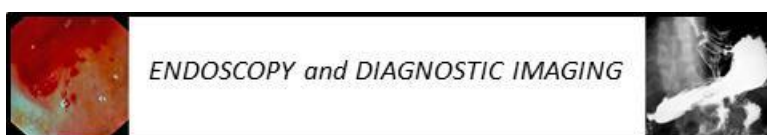
Printed with permission from: Brugge WR, 2008 ACG Annual Postgraduate course book.

Recent Updates: Differentiate between Focal Autoimmune Pancreatitis and Pancreatic Cancer

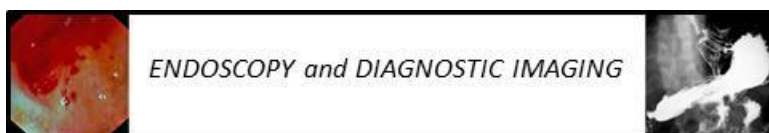
- It may be difficult to distinguish between autoimmune pancreatitis (especially the focal variety) and pancreatic cancer. An antibody to a PBP-like protein of H.Pylori is found in over 90% persons with autoimmune pancreatitis, and in less than 10% of those with pancreatic cancer (NJEM 2009, 361: 2135-2142).
- Pancreatic Cancer
 - 5th leading cause of cancer-related death
 - 5-year survival: 3–5%
 - Usually presents late
 - After successful surgery: 20%
 - Low percentage is resectable
 - Early Detection

Practice Pointers:

- SMAD4 / DPC4 Gene
 - Downstream regulator of the TGF- β signalling pathway
 - Inactivated in ~55% of pancreatic carcinomas
 - Relatively specific for pancreatic carcinoma
 - A late event in the pancreatic tumor progression model
 - Immunohistochemical labeling for DPC4 protein closely mirrors DPC4 gene status
- Pancreatic ductal adenocarcinoma
 - 70–75% in head of pancreas
 - 60% originate around main pancreatic duct
 - 40% in upper dorsal part, adjacent to common bile duct – (may leave main pancreatic duct unaffected)
 - Variable figures for multifocality (0–25%) ~15%
 - in part due to intraductal spreading



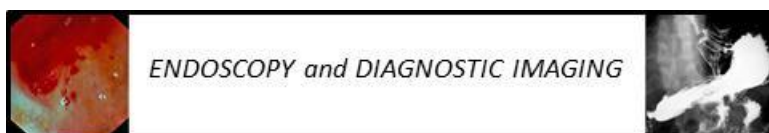
- Cause of local recurrence after resection? (usually from residual tumor nests in the tissues surrounding the pancreatico-jejunal anastomosis)
- Risk factors
 - Smoking – possibly accounts for a quarter of all cases of pancreatic cancer
 - Diabetes mellitus?
- Genetic predisposition
 - BRCA2 germline mutation carriers have a 10-fold higher risk of developing pancreatic cancer → possibility for screening?
 - FAMMM (familial atypical multiple mole melanoma) patients with CDKN2A/p16 or CDK4 mutations have a dysregulated G1/S checkpoint and variably increased PCa risk
 - Hereditary pancreatitis patients with mutated cationic trypsinogen gene PRSS1 (present in 70%) develop cancer in 40% by age 70, with smokers having a substantially higher risk
 - HNPCC (hereditary non-polyposis colorectal cancer) with mutation in one of the DNA mismatch repair genes. This leads to microsatellite instability seen in 3% of pancreatic cancer
 - Peutz-Jeghers leads to mutation in the LKB1/STK11 tumor suppressor gene seen in 4% of pancreatic cancer
 - Familial pancreatic cancer with so far unidentified germline mutation
- Familial inherited predisposition
 - Individuals with 2 or more first degree relatives with pancreatic adenocarcinoma
 - Individuals with 1 first degree relative who developed pancreatic adenocarcinoma before age 50
 - Individuals with 2 or more second degree relatives with pancreatic adenocarcinoma, one of whom developed the cancer at an early age.
 - Special familial kindred (risk x 100); EUS chronic pancreatitis like lesions
- Drugs/diet
 - Smoking
 - Alcohol
 - High saturated fatty acid diet
 - Low vegetable diet
 - Low vitamin diet
 - Exposition to Dichlorodiphenyltrichloroethane or dieldrin (7-fold higher risk)



- Miscellaneous
 - Diabetes mellitus
 - Cystic fibrosis
 - Fanconi anemia
 - Familial adenomatous polyposis
 - Ataxia telangiectasia
 - Li-fraumeni syndrome
 - Neuroendocrine tumours

Useful background: The genetic diseases/associations of pancreatic cancer

- Hereditary pancreatitis
 - Cationic trypsinogen (CT)
 - CF
 - SPINK
- Polyp syndromes
 - FAP
 - HNPCC-Lynch mismatch MLH1, MSH2, BRCH2
 - HNPCC
 - Peutz-Jeghers syndrome
 - Cowden syndrome
 - Familial atypical mole and multiple melanoma (FAMMM): germline p16 mutation
 - Hereditary breast cancer: germline BRCA2 mutation
 - Oncogenes - K-RAS mutations (90%) and p53 (70%) indicate tumor induction by exogenous carcinogens
 - Inactive tumour suppression gene (p59, p16 [DKN2A])
 - Familial pancreatic cancer
 - Familial ovarian and breast cancer
- Drugs/Diet
 - Risk factors are smoking, alcohol, and high-saturated fat/low vegetable/low vitamin diet
 - 7-fold increased risk after exposition to dichlorodiphenyltrichloroethane or deviates (e.g. ethylene)
- Metabolic
 - Chronic pancreatitis
 - Diabetes
 - Partial gastrectomy
- Miscellaneous
 - Diabetes mellitus



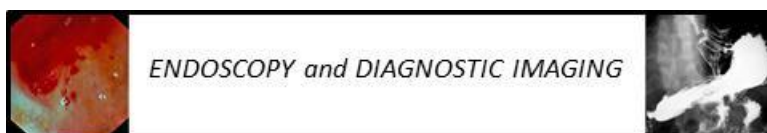
- Cystic fibrosis
- Fanconi anemia
- Familial adenomatous polyposis
- Ataxia telangiectasia
- Li-fraumani syndrome
- Neuroendocrine tumors

Useful background: The possible techniques for screening of high risk individuals for pancreatic cancer

- Non-invasive
 - Stool or blood analysis for gene mutations
 - Computed tomography
 - Positron emission tomography
 - Magnetic resonance imaging
- Invasive
 - Endoscopic ultrasonography
 - Endoscopic pancreatoscopy
 - Endoscopic retrograde cholangiography for brush cytology or collection of pancreatic juice or bile for cytology & mutation analysis
 - Duodenal/pancreatic juice collection for mutation analysis

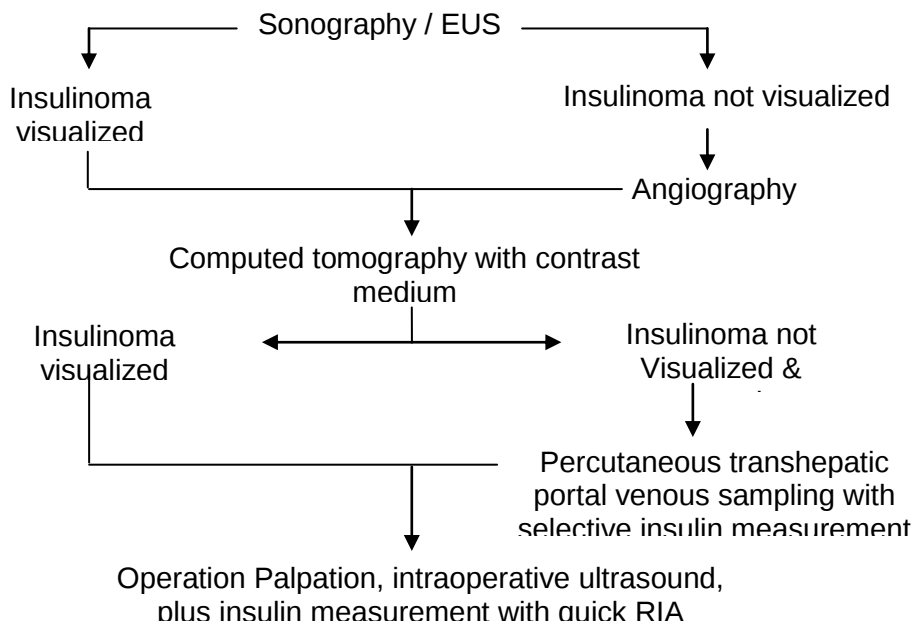
Useful background: The scientific rationale for Pancreatic Cancer – Screening/Surveillance

- Mutational activation of KRAS is early event in 90% and detectable in plasma, stool, duodenal aspirate, pancreatic juice and brush cytology (false positive in hyperplastic lesions)
- Increased telomerase activity in pancreatic juice
- Loss of heterozygosity for tumor suppressor genes p16, p53 and MADH4
- Start screening at least a decade before the earliest age of onset in an affected family or at age 50 except for hereditary pancreatitis
- Molecular Markers to possibly Improve of Pancreatic Cancer. Early Diagnosis
- Oncogenes:
 - K-ras 80–90%
- Tumor suppressor genes:
 - P16 80–100%
 - P53 50–70%
 - DPC4 50–70%
- The imaging modalities for pancreatic cancer
 - Site space



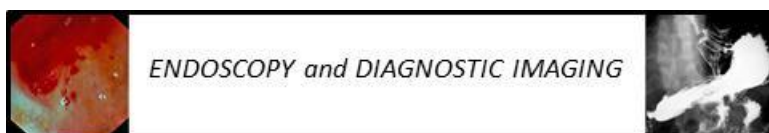
- 10-20% : localized disease
 - 40% : locally advanced pancreatic cancer
 - 40% : metastatic disease
- US/Doppler
 - Spiral CT
 - Echoendoscopy
 - MRI
 - MCRP
 - ERCP
 - Angiography

Useful background: Organic hyperinsulinism

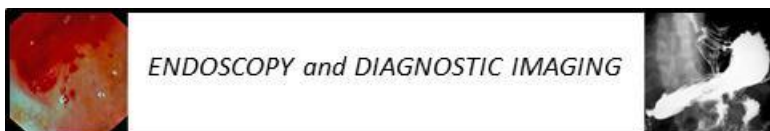


Useful background: Clinicopathologic classification of endocrine tumors of the pancreas

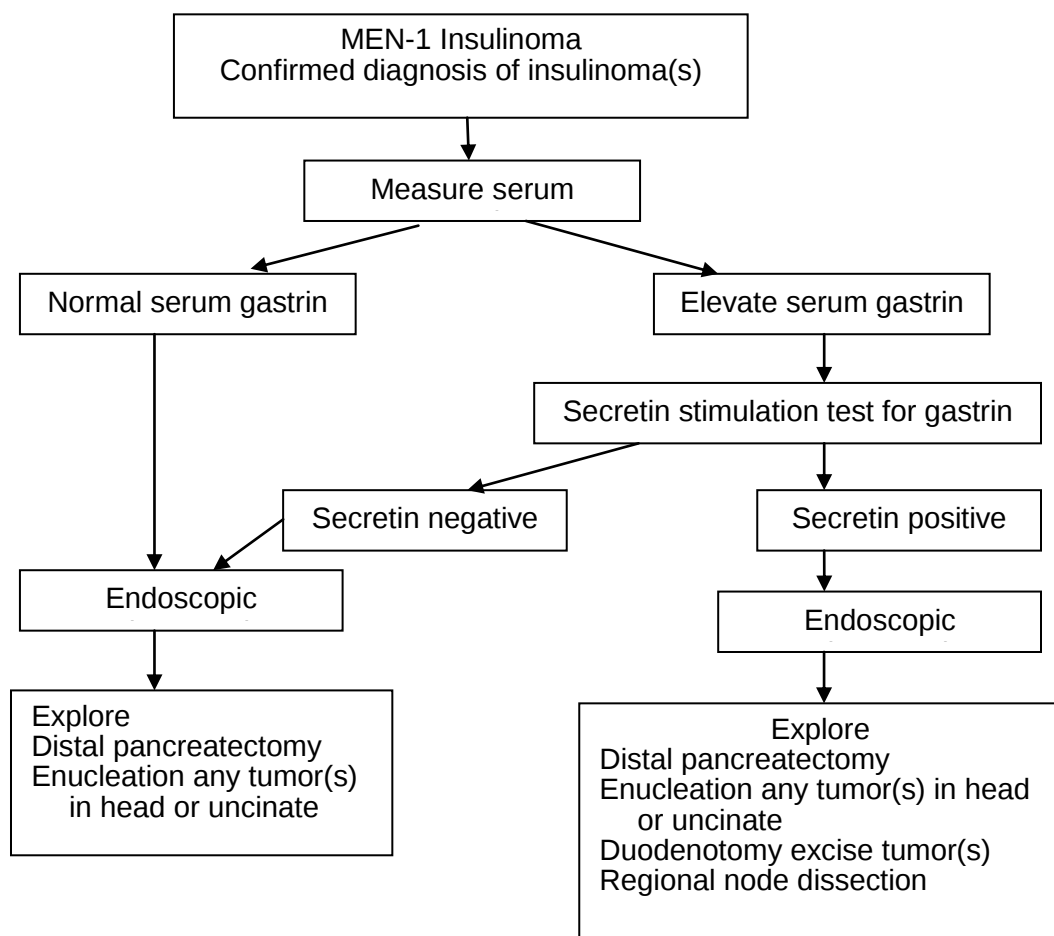
- Well-differentiated endocrine tumor
 - Benign behaviour: non-functioning, confined to pancreas, non-angioinvasive, < 2 cm in size,
 - Functioning - insulinoma
 - Non-functioning



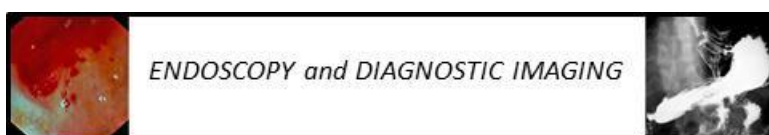
- Uncertain behaviour: confined to pancreas, $\geq 2\text{cm}$ in size or angioinvasive
 - Functioning gastrinoma, insulinoma, VIPoma, glucagonoma, somatostatinoma or other tumors*
 - Non-functioning
- Well-differentiated endocrine carcinoma
 - Low-grade malignant with gross local invasion and/or metastases
 - Functioning gastrinoma, insulinoma, glucagonoma, VIPoma, somatostatinoma or other tumors*
 - Non-functioning
- Poorly differentiated endocrine carcinoma
 - High grade malignant (small to intermediate cell) carcinoma



Useful background: MEN-1 Insulinoma: Confirmed diagnosis of insulinoma(s)

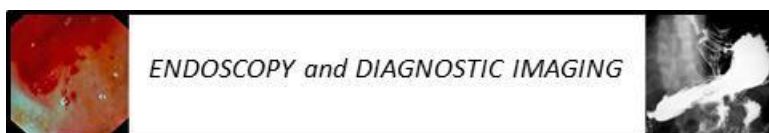


Printed with permission: Thompson NW. The surgical management of hyperparathyroidism and endocrine disease of the pancreas in the multiple endocrine neoplasia type 1 patient. *J Intern Med* 1995; 238:, 269-280 (Figure 7).



Useful background: Clinical syndromes associated with pancreatic islet cell tumors

Name of syndrome	Signs and/or symptoms	Hormone/Peptide Marker
Gastrinoma (Zollinger-Ellison Syndrome)	Abdominal pain Dyspepsia	Gastrin
VIPoma/ (Verner Morrison Syndrome)	Severe watery diarrhea Hypokalemia, dehydration	Diarrhea VIP
Insulinoma	Hypoglycemic symptoms	Insulin
Glucagonoma	Rash, Anemia, weight loss, Diabetes, Glucose intolerance, Thromboembolic disease	Glucagon
Somatostatinoma	Diabetes Mellitus, Cholelithiasis Diarrhea, Steatorrhea	Somatostatin
GRFoma	Acromegaly	GRF
Ppoma	Weight loss, Abdominal mass often asymptomatic	PP
CCKoma	Hypersecretion of pancreatic enzymes Incomplete filling of fasting gallbladder	CCK
Neurotensinoma	Flushing, Diarrhea	Neurotensin
Ulcerogenic Tumor acid Syndrome with Non-Peptide Gastrin Secretagogue	Dyspepsia	Non-gastrin secretagogue



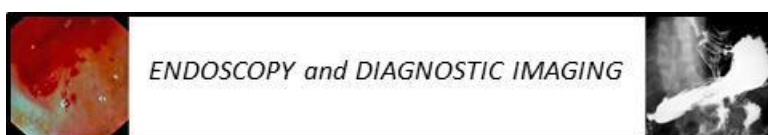
Useful background: Results of long-term treatment of patients with the carcinoid syndrome with octreotide

- Complete disappearance of flushing episodes in +/- 60%
- >50% reduction in the frequency and/or severity of the flushing periods in >85%
- Disappearance of diarrhea in >30%, >50% improvement of diarrhea in >75%
- Significant reduction of urinary 5-HIAA in >50%
 - Objective transient antineoplastic effects in +/- 0%
 - Increase of median progression-free survival from 3.5 to 15 months

Diagnostic imaging

Useful background: Pancreatic adenocarcinoma

- Contrast – enhanced CT
 - Mass
 - Large
 - Hypoattenuating (dark) in pancreatic phase, but isoattenuating in portal venous phase
 - Some pancreatic adenocarcinomas are isoattenuating
 - Uncinate process
 - Rounded
 - Hypoattenuated
 - Staging
 - Local extension
 - Encasement of vessels
 - Occlusion of splenic vein
 - Deformity of superior mesenteric vein (SMV)
 - Multiple collaterals
 - Hepatic metastases
 - Lymphatic / peritoneal spread
 - CT superior to Doppler ultrasound for staging
- Ultrasound
 - Mass
 - Hypoechoic
 - Poorly defined
 - Ducts
 - Dilated

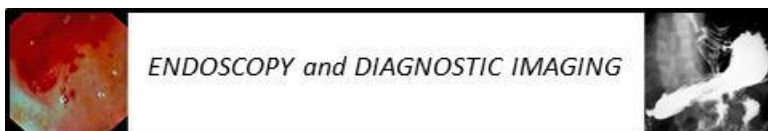


Distinguishing diagnosis: solid, hypoechoic pancreatic mass (es)

- Adenocarcinoma
- Metastases
- Islet cell tumors
- Lymphoma
- Focal pancreatitis

Useful background: Pros and cons ultrasound vs. CT scanning in pancreatic disease

- Ultrasound
 - Superior for biopsy, since
 - Overlying air-filled loops of bowel may be displaced
 - Real-time visualization allows for better navigation around blood vessels
- Contrast –enhanced CT scan
 - Superior to ultrasound for staging
 - Contrast CT pancreatic phase
 - Hypoattenuation, suggests pancreatic adenocarcinoma
 - Dual – phase (pancreatic plus portal venous phase is recommended)
- Useful to detect
 - Hepatic metastases
 - Local lymphadenopathy
- MRI
 - T₁ – weighted – hypointense (dark)
 - T₂ – weighted – hyperintense (white)
 - Gadolinium
- MRCP
 - Hypointense mass

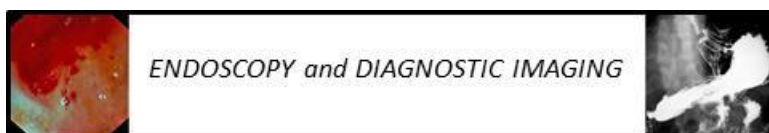


Useful background: Identifying in difficult to find pancreatic tumors

- Small tumors – T_1 – weighted MRI with fat saturation – for small tumors (hypointense)
- Secondary findings
 - Small tumors, or isoattenuating large pancreatic adenocarcinomas
 - Dilation of proximal pancreatic and biliary ducts
 - Atrophy of area of pancreas
 - Encasement of vessels
 - Deformity of superior mesenteric vein (SMV) loss of, cuff of fatty tissue around SMV
 - Local
 - Lymphadenopathy
 - Peritoneal carcinomatous
 - Ascites

Useful background: Islet cell tumors (ICT)

- Ultrasound / endoscopic ultrasound
 - Hypoechoic mass (must have a water-filled stomach)
 - Intraoperative ultrasound is ~ 99% sensitive for islet cells tumor (ICT)
 - Rim of hyperenhancing tissue
 - Metastatic islet cell tumor
 - Echogenic (white), with posterior acoustic shadowing
 - Rare cystic ICT
 - Septation
 - Nodule
- Contrast – enhanced CT
 - Hyperenhancing (white) mass in arterial phase
 - Solid / cystic
 - Single / multiple
 - “gastrinoma triangle”



Useful background: Junction cystic duct / CBD

- Junction Neck / body of pancreas



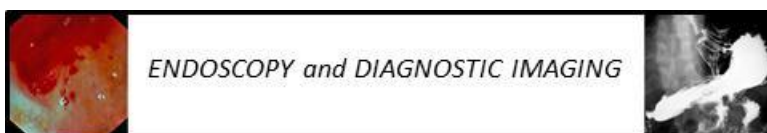
- Ampulla of Vater
- Small, multiple, well defined
 - May be extrapancreatic – gastric antrum proximal duodenum, lymph nodes in triangle”
 - Hepatic metastases may become isoattenuating
- Upper GI barium study
 - Thick folds
 - Peptic ulcers
 - Excess fluid in stomach / duodenum

Distinguishing diagnosis: Islet cell tumor (ICT) metastasis to livers vs. hepatic hemangioma on ultrasound

	Echogenic	Posterior Acoustic Shadowing
Hemangioma	+	-
ICT	+	+

Useful background: Octreotide scan uptake by somatostatin-receptor rich islet cell tumor

- MRI
 - T₁
 - Weighted
 - Masses – hypointense (dark)
 - T₂
 - Weighted
 - Masses – hypertensive (white)
 - Liver metastases – fluid – filled layers



Distinguishing diagnosis: Ductal Adenocarcinoma vs. Islet Cell Tumors

Features	Ductal Adenocarcinoma	Islet cell Tumor
Size	≤ 4 cm	0.5 mm to 100 mm
Vascularity	↓	↑
Vascular Encasement	++++	+
Calcification	+	++++
Duct dilation	++++	+

Useful background: Lymphoma

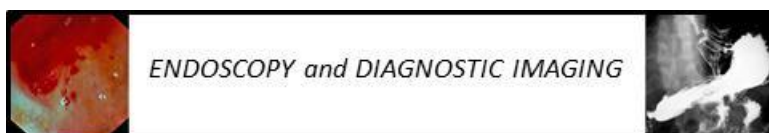
- Contrast – enhanced CT
 - Mass
 - Large
 - Enhancement
 - Homogeneous

Distinguishing Diagnosis

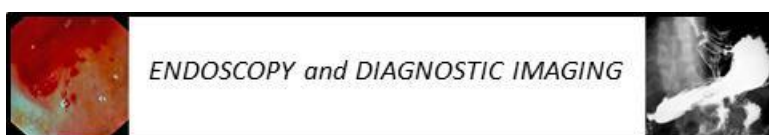
	Primary Lymphoma	Ductal Adenocarcinoma	Non-functioning ICT
Circumscribed	+	-	
Vascular encasement	-	+	
Pancreatic / Bile duct Obstruction	-	+	
Homogeneous	+		-
Hyperenhancement	+	-	+
Calcification	-		+

Useful background: Metastases to pancreas

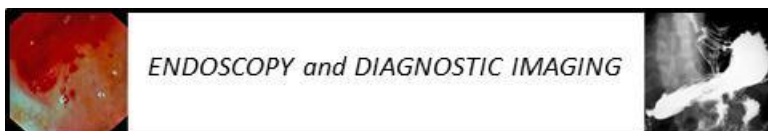
- Contrast – enhanced CT
 - Pancreatic phase
 - Masses
 - Multiple
 - Hyperenhancing (white)
 - Primary sites: kidney, melanoma, lung, soft tissue sarcomas



- Ultrasound
 - Masses
 - Hypoechoic
 - Often associated intra- abdominal lymphadenopathy
- Cystic Tumor of the Pancreas
 - Serous cystadenoma
 - Mucinous cystadenoma
 - Intraductal pancreatic mucinous neoplasm (IPMN)
 - Pseudocyst
 - Von Hippel-Lindan disease
 - Abscess
 - Cystic islet cell tumor
 - Solid and papillary epithelial neoplasm
- Serous Cystadenoma
- Contrast – enhanced CT
 - Mass
 - Multiple (≥ 6), small (< 2 cm) cysts
 - Septal calcification
 - Central scan
 - Low attenuation (dark)
 - Circumscribed
 - Septae – thin (“honey comb” – like)
- Ultrasound
 - Cysts, or solid appearance if multiple small cysts result in numerous acoustic interfaces
 - MRI without contrast
 - T_1 –weighted images
 - Low signal intensity (dark)
 - T_2 –weighted images
 - High signal intensity (white)
 - Duct dilation
- Mucinous cystadenoma
- Contrast – enhanced CT
 - Mass
 - Few (, 6), large (> 2 cm) cysts
 - Septae – thick
 - Nodules in wall; thick septae and mural nodules suggest possible mucinous cystadenocarcinoma



- Enhancing
- Pancreas Divisum
- ERCP
 - Drainage
 - Dorsal pancreas
 - Duct of Santorini accessory papilla
 - Duct of Wirsung major papilla
 - Small, branching duct
- Ascites
- Ultrasound
 - An echoic fluid
 - Exudatic / transudate
 - Blood, bile, lymph, pus, urine
 - Site
 - Early
 - Hepatorenal access space (Morrison pouch)
 - Pelvic cul-de-sac
 - Late
 - Entire free space of abdominal cavity
 - Complicated
 - Infection, bleeding, malignancing
 - Diffuse low-level echoes
- Contrast – enhanced CT
 - Abscess
 - Fluid collection
 - Collection surrounded by thick, enhancing rind
 - Bubbles of air
 - Multiple septae (loculated)
 - Compression of bowel (no displacement)
 - Blood (hemoperitoneum)
 - High density material
 - Layers of different attenuation
- Peritoneal Carcinomatosis
- Contrast enhanced CT
 - Enhancing (dark) nodules along the surface of the peritoneum
 - Nodular thickening of the omentum
 - Omental “caking” (omentum replaced by tumor)
 - Bowel displaced posteriorly



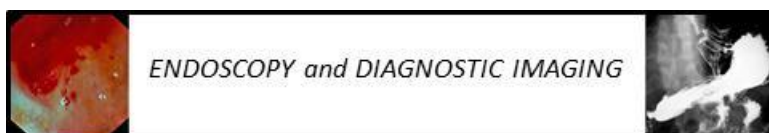
- Common sites
 - Pelvic cul-de-sac
 - Right paracolic gutter
 - Root of mesentery at the ileocecal junction
 - Sigmoid mesocolon
- Identical appearance for peritoneal perisigmoid diverticular abscess TB, and malignant mesothelioma of peritoneum
- Primary
 - GI
 - Pancreas
 - Liver
 - Gallbladder
 - Stomach
 - Ovary

Useful background: Intraductal pancreatic mucinous neoplasm (IPMN)

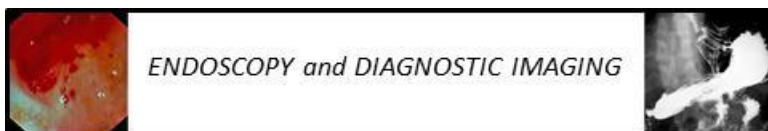
- Contrast – enhanced CT
 - Mass arises either in pancreatic ducts or in isolation from ducts
 - Uni- or multiocular
 - Dilated ducts (from mucin)
 - Small villous IPMNs look like “frondlike enhancing filling defects within the dilated pancreatic duct”
 - Atrophy of parenchyma
 - Calcification
 - Solid tissue-like attenuation from mucin within ducts
- ERCP
 - Standard for diagnosis
 - Filling defects in ducts
 - Duct dilation
 - Cyst may fill with contrast from a duct (communication)
 - Mucin seen dripping out papilla of Vater

Useful background: Contrast – enhanced CT appearance of carcinoid tumor, or retractile mesenteritis:

- Calcified mesenteric mass
- Radiating strands
- Thickening of or mass in adjacent bowel wall
- Mesenteric Non-Hodgkin Lymphomas
- Contrast – enhanced CT
 - Mesenteric mass
 - Lobulated



- Confluent
 - May surround (encase) SMA/SMV
 - Encasing may cause “sandwich” or “hamburger” sign
 - Associated
 - Adenopathy
 - Retroperitoneal
 - Inguinal
 - Splenomegaly
 - Cavitory Mesenteric Lymph Node Syndrome (CMLNS)
 - Contrast – enhanced CT
 - Cystic mesenteric masses
 - Complication of celiac disease
 - Multiple
 - Size 2 cm to 7 cm
 - Filled with chylous fluid
 - Thin rim of fibrous tissue
 - Low-density (dark) mesenteric lymph nodes on contrast – enhanced CT
 - CMLNS
 - Treated lymphoma
 - Whipple disease
 - Infection
 - TB
 - MAC
 - Histoplasmosis
 - Polycystic Kidney Disease
 - MRI
 - T₁ – weighted
 - Cysts
 - Diffuse
 - High signal intensity
 - Cysts may appear in kidney, liver, as well as pancreas
 - Von Hippel – Lindau disease
 - Contrast enhanced CT
 - Cysts
 - Tiny
 - Numerous
 - Association with
 - Serous cystadenomas
 - Islet cell tumors of pancreas
- * aka diffuse pancreatic cystosis

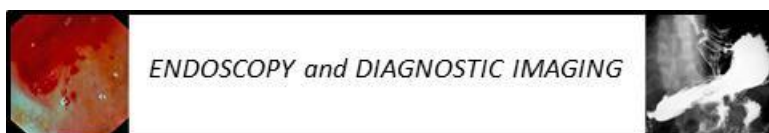


Useful background: Annular pancreas

- Contrast – enhanced CT
 - Low attenuation
 - Peripancreatic tissue stranding
- ERCP
 - Ventral pancreatic duct circles around the duodenum
 - Pancreatic tissue may encircle the duodenum

CYSTIC FIBROSIS

- Non-GI/Hepatobiliary manifestations of cystic fibrosis in the adult.
- Respiratory
 - sinusitis
 - nasal polyposis (secondary to mucous membrane hypertrophy)
 - lower respiratory infections
 - bronchiectasis
- GU
 - male infertility (sterility; congenital absence of vas deferens, epididymis, and seminal vessels)
 - female infertility (increased viscosity of vaginal mucous)
- Nutrition
 - Clubbing
 - Short stature
- Premature death
- Reproductive
 - Female gender
 - Increased viscosity of vaginal mucus and decreased fertility
 - Male gender
 - Sterility: absence of ductus deferens, epididymis and seminal vesicles
- Skeletal
 - Retardation of bone age
 - Demineralization
 - Hypertrophic pulmonary osteoarthropathy
- Ophthalmic
 - Venous engorgement
 - Retinal hemorrhage
- Other
 - Salt depletion through excessive loss of salt via the skin



- Heat stroke
- Hypertrophy of apocrine glands

Adapted from: Whitcomb DC. *Sleisenger & Fordtran's gastrointestinal and liver disease: Pathophysiology/Diagnosis/Management* 2006: pg. 1214.

Diagnostic Imaging

Bile Duct

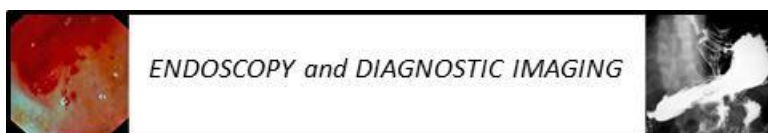
Useful background: Inflammatory disease

- Primary Sclerosing Cholangitis (PSC)
- ERCP / MRCP, PCC percutaneous cholangiogram
 - Band like narrowing of bile ducts
 - 80% involve extra- and intrahepatic ducts (IND), 20% only INDs
 - Strictures
 - Segmental
 - Non-uniform (ie, random segmental strictures)
 - 1 to 2 cm long
 - “pruning” of IHDs (from obstruction)
 - May be a “dominant” structure (suggesting cholangiocarcinoma)
 - Diverticulae
 - Beaded appearance of ducts
 - Mucosa – irregular
 - Intrahepatic “small-duct” disease may look like early PBC

*MRCP does not have as good spatial resolution as does ERCP, and may miss subtle changes such as mural irregularity; unlike ERCP, MRCP visualizes beyond a strictured duct

Useful background: Contrast-enhanced hypoattenuating (dark)

- CT
 - Delayed contrast-enhanced
 - Hypovascular
 - Enhancing mass (fibrotic [desmoplastic])
 - Lobular atrophy (from chronic biliary obstruction)
 - Metastases
 - Portacaval
 - Peripancreatic
 - Metastatic lesions to liver cannot be distinguished from intrahepatic cholangiocarcinoma



Useful background: Cholangiocarcinoma (CC)

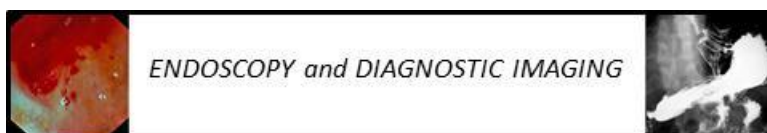
- MRI
 - T₁- weighted
Hypointense (dark)
 - T₂- weighted
Hyperintense (white) mass
Heterogeneous
Multiple dilated ducts
Multiple dilated ducts may converge to central mass
- ERCP, MRCP
 - Intraluminal Filling Defect
 - Infiltrating (thickening of duct wall)
 - Polypoid
 - Extension (along duct into liver, or into vessels)
 - Commonly at bifurcation of R/L hepatic ducts ("Klatskin" type)
 - When in peripheral ducts – proximal duct dilation

.....
Distinguishing features:

.....
Intrahepatic Cholangiocarcinoma
.....
Cannot be distinguished from metastatic lesions to liver
.....
HCC is hypervascular, CC is not
.....
Biliary cystadenoma
.....

Useful background: Primary biliary cirrhosis (PBC)

- T-tube cholangiogram
 - Intrahepatic ducts ("small – duct" disease)
Early in course / PBC
Close together ("crowded")
"pruned" ("large – duct" disease)
 - Extrahepatic ducts
Tortuous
Deformed
- Unenhanced CT
 - Same findings as with T-tube cholangiogram, except the intrahepatic ducts are affected early (crowded, pruned), and the extrahepatic ducts are affected late (tortuous, deformed)
 - Hepatic abnormalities in keeping with cirrhosis
 - Lymph nodes enlarged in porta hepatis
 - Early intrahepatic "small-duct" disease may look like PSC



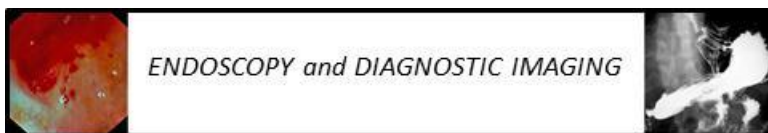
- AIDS – Associated Cholangiopathy
 - Changes of segmental strictures similar to pSC
 - PSC – like changes plus papillary stenosis, or papillary stenosis alone suggests AIDS – associated cholangiopathy is due to infection of the biliary tree with CMV or Cryptosporidium
- Bacterial Cholangitis
 - Ducts
 - Irregular
 - Strictures
 - Sac-like filling defects (abscesses) communicating with bile ducts
 - Fluid in abscesses

Useful background: Oriental cholangiohepatitis

- Percutaneous Cholangiogram, CT, Ultrasound
 - Intra – (IHDs) / Extrahepatic Duct pigmented Stones
 - Duct dilation
 - Focal strictures
 - Straight, rigid IHD
 - Tapering (pruning) of ducts
 - Decreased arborisation of ducts
 - Gallstones
- MRI
 - T₁ – weighted
 - Dark tubular structures
 - T₂ – weighted
 - Dark tubular structures
 - Gadolinium – enhanced
 - Stones in dilated ducts

Useful background: Masses and filling defects

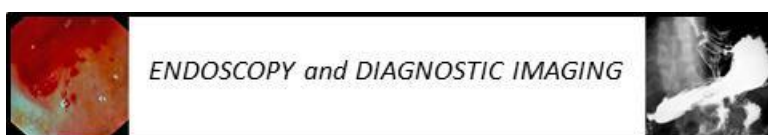
- Choledocholithiasis
- ERCP, MRCP, contrast – enhanced CT
 - Duct dilation (extra - / intrahepatic ducts)
 - Filling defects in ducts
 - Colouring of stones depends on their composition
 - May be fluid around stone
 - Target sign
 - Fluid all around stone
 - Crescent sign
 - Fluid around part of stone



- Pseudocalculus
 - Only the superior part of the filling defect outlined in pseudocalculus (caused by spasm of sphincter of Oddi), whereas both superior and inferior parts of the filling defects seen with stone
- Papillary Stenosis
- Transhepatic Cholangiogram
 - Narrowing of distal portion of common bile ducts (CBD) dilation of extra- / intrahepatic bile ducts

Useful background: Mirizzi syndrome

- ERCP, CT, ultrasound
 - Filling defects (stroma) impacted in cystic duct or head of gallbladder secondary narrowing of common bile duct (CBD) or, common hepatic duct (CHD) by inflammatory stricture.
- Extrinsic Compression
 - Narrowing long segment of common hepatic duct
 - Hilar lymphadenopathy
- Intraluminal Masses
- Multiple Solid Filling Defects
 - Stones
 - Sludge (balls)
 - Mucous (Plugs)
 - Blood (clots)
 - Cholangiocarcinoma
 - Biliary papillomatosis high risk of malignant degeneration mucus filling defects
- Miscellaneous Condition of the Bile Ducts
 - Cystic duct
 - Bile leak
 - Choledochal cysts



Useful background:

- Abnormalities of Cystic Duct (CD)
 - Absent
 - Low insertion
 - Long CD running parallel to CBD
 - CD inserted into R. hepatic duct
 - CD inserted into common hepatic duct at bifurcation of R/L hepatic ducts

Useful background: Definitions of choledochal cysts

- Congenital cystic dilations of the bile ducts
 - Type I
 - Choledochoceles : “protrusion of a dilated intramural segment of the common bile duct into the duodenum”

Useful background: Caroli disease

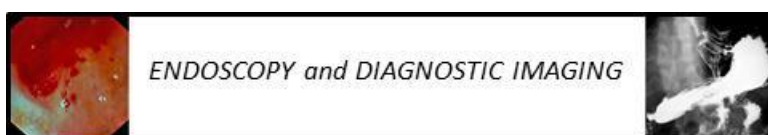
- ERCP/MRCP multiple, marked dilations of intrahepatic bile ducts
- MRI
 - T₁ – weighted
 - Multiple, marked dilations of intrahepatic bile ducts (dark)
 - T₂ – weighted
 - Same as T₁ – weighted, but white
 - Dynamic contrast
 - Enhanced MRI
 - Heterogeneous enhancement in early arterial phase of contrast enhancement (ie, HCC)
 - Marked increase risk of HCC

GALLBLADDER

- Inflammatory Conditions

Useful background: Acute cholecystitis

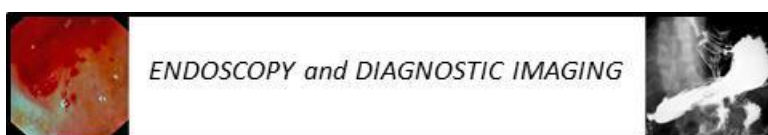
- Definition: Acute inflammation of the gallbladder wall due to obstruction of the cystic duct by gallstones
- Ultrasound
 - Lumen-cholelithiasis or sludge



- Wall-thickening / edema
 - Striations
- Murphy sign positive when using ultrasound probe
- Decreased hepatic echogenicity (dark) around gallbladder (“perihepatitis”)
- Pericholecystic fluid
- Cholescintigram
 - Non-visualization of gallbladder up to 4 hours
 - Enhanced uptake of tracer into the liver near the inflamed gallbladder (perihepatitis)
- Gangrenous cholecystitis
- Ultrasound contrast – enhanced CT
 - Wall – thickening (intramural edema; white [water attenuation])
 - Lumen
 - Striated appearance
 - Echogenic (light) filling defects (sloughed gangrenous mucosa)
 - Pericholecystic
 - Fluid collection (from perforation)
 - Fluid may collect in “Morrison pouch” (posterior subhepatic space)
 - May see associated gallstones
- Emphysematous cholecystitis
- Abdominal plain radiograph
 - Air
 - In gallbladder wall
 - In surrounding tissue (extraluminal air in pericholecystic tissue)
 - Produced from gas-forming clostridium perfringens
- Ultrasound
 - Air in gallbladder wall: posterior “dirty” shadowing echogenic (white) rim

Useful background: Acalculous cholecystitis

- Definition: Acute inflammation of the gallbladder wall without obstruction of the cystic duct by gallstones
- Ultrasound, CT, cholescintigraphy
 - Inflammatory changes in wall of gallbladder (similar to acute cholecystitis with stones)
 - Cystic duct is not obstructed by stones



- Chronic cholecystitis
 - Lumen-stones
 - Wall-thickening and striations
 - May be difficult in imaging to distinguish acute from chronic cholelithiasis
 - May be associated with “porcelain” gallbladder, milk of calcium bile, or carcinoma
- “Porcelain gallbladder”
- Contrast-enhanced CT
 - Wall-calcification
 - Calcification may be linear or punctate
 - High risk (25 to 90%) of associated gallbladder carcinoma
- Ultrasound
 - Echogenic arc
 - “clean” posterior shadowing

.....

Distinguishing features:

Porcelain gallbladder

“clean” posterior acoustic shadowing: single, thin echogenic (white) line

Emphasematous gallbladder

“dirty” posterior shadowing

Gallbladder filled with stones

“wall-echo-shadow”: echogenic line

Lucency

Echogenic line

Cholelithiasis

“clean” posterior shadowing plus echogenic arc acoustic

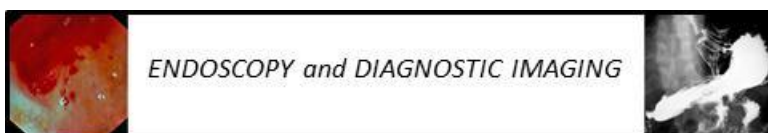
Milk of calcium bile

Gallbladder and cystic duct are opaque on abdominal plain radiograph, and hyperattenuated (white) on unenhanced CT

.....

Useful background: Masses and Filling Defects

- Gallstones
- Abdominal plain radiograph may be visible if the stones contain a large amount of calcium.



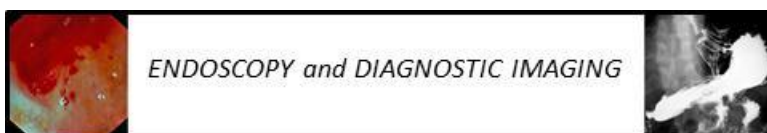
- Ultrasound
 - Filling defects in lumen of gallbladder
 - Round
 - Echogenic
 - Dependent portion
 - Wall-echo shadow
 - Echogenic (white) wall
 - Hyperechoic (dark) line of fluid
 - Echogenic (light) line of “clean” posterior acoustic signalling
 - “clear” posterior acoustic shadowing (absent with sludge balls)
 - Performance characteristics: Sensitivity 95%
Specificity 99%
- Sludge
- Ultrasound
 - Echogenic (white) bile
 - Dependent layering (unless “tumefactive” sludge)
 - Tumefactive sludge – a ball of sludge
 - No posterior acoustic shadowing

.....
Distinguishing features on ultrasound:

	<u>Stones</u>	<u>Sludge</u>	<u>Polyp / Tumor</u>
“clean” posterior acoustic shadowing	+	-	-
Mobility	+	+	-
Internal blood flow	-	-	+

.....

- Polyps
- Ultrasound
 - Intramural filling defects
 - Multiple / single
 - Usually < 1 cm (when > 1 cm, suspect carcinoma)
 - Non-mobile
 - No posterior acoustic shadowing
 - Internal blood flow
 - Blood flow in mass
 - Melanoma metastatic to the gallbladder looks similar
- Adenomyomatous
- Ultrasound
 - Multiple echogenic foci in wall



“comet-tail” artifacts (crystals of cholesterol trapped in the Rokitansky – Aschoff sinuses [herniation of mucosa into the muscle layer of the wall of the gallbladder])

- May be in non-dependent part of gallbladder
- Thickened wall
 - Diffuse (diffuse thickening of gallbladder wall mimics acute / chronic cholecystitis)
 - In the fundus / rest of gallbladder
 - Narrows lumen of gallbladder
 - Filling defects in lumen near fundus of gallbladder

➤ Carcinoma

- Ultrasound, contrast enhanced CT
- Hypoechoic (white) mass
 - Infiltrating (scirrhous type, infiltrates into liver)
 - Polypoid grows into lumen
 - Blood flows into mass
 - Usually > 1 cm
 - Distention of gallbladder

SO YOU WANT TO BE A GASTROENTEROLOGIST!

Q1. In the presence of obstructive jaundice, a palpable gallbladder is not due to cholelithiasis. What are the exceptions to this clinical “rule”?

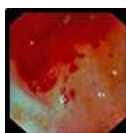
A1. Stones in the cystic duct, or Hartmann’s pouch.

Q2. Splenomegaly accompanies hepatomegaly in persons with portal hypertension. What are the exceptions to this clinical “rule”?

A2. Congenital asplenia
 Post-surgical asplenia
 Splenic vein thrombosis
 Multiple splenic vein infarctions

Q3. In most patients with viral hepatic, the liver is usually enlarged and tender whereas the spleen is enlarged and none tender. Which hepatic infection instead causes a large, tender spleen and non-tender hepatomegaly?

A3. EPV (Epstein Barr virus)



Miscellaneous conditions

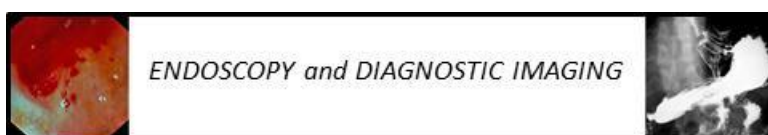
- Phrygian Cap
- Definition: A congenital abnormality of the fundus of the gallbladder causing folding of the wall
- Ultrasound
 - Thin, white infolding of the wall of the fundus of the gallbladder
 - High attenuation (dark) line projecting into lumen of the gallbladder
- Contrast enhanced CT
 - Focal narrowing in the wall of the fundus of the gallbladder

Useful background: Distinguishing features or ultrasound / contrast – enhanced CT

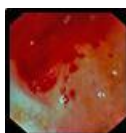
	Phrygian cap	Focal adenomyomatosis
Fundus	+	Anywhere
Membrane	Thin	Thick
Annular	-	+

Useful background: Thickening of wall of gallbladder (> 3 mm)

- Non cystic
 - Technique
 - Non-distention of gallbladder
 - Gallbladder
 - Acute / chronic cholecystitis
 - Adenomyomatosis
 - Liver
 - Hepatitis
 - Cirrhosis
 - Portal hypertension
 - Pancreas
 - Pancreatitis
 - Hypoproteinemia
 - Lymphatic obstruction
- Cystic ultrasound Doppler – ultrasound, MRI
 - Cystic spaces in wall of gallbladder
 - Wall thickened
 - Collateral vessels possible signs of portal hypertension, portal vein thrombosis



- Heart (CHF)
- Failure
 - Kidney (CRF)
 - Liver

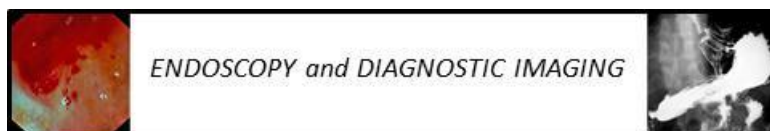


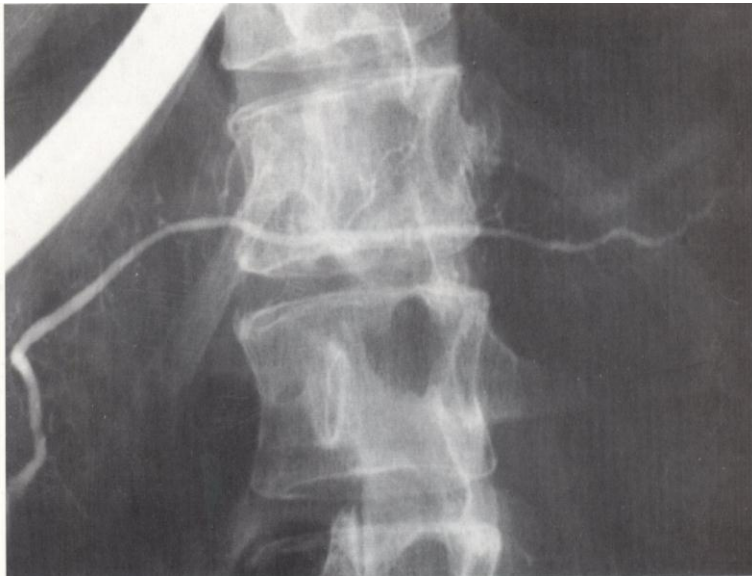
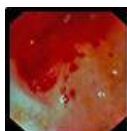
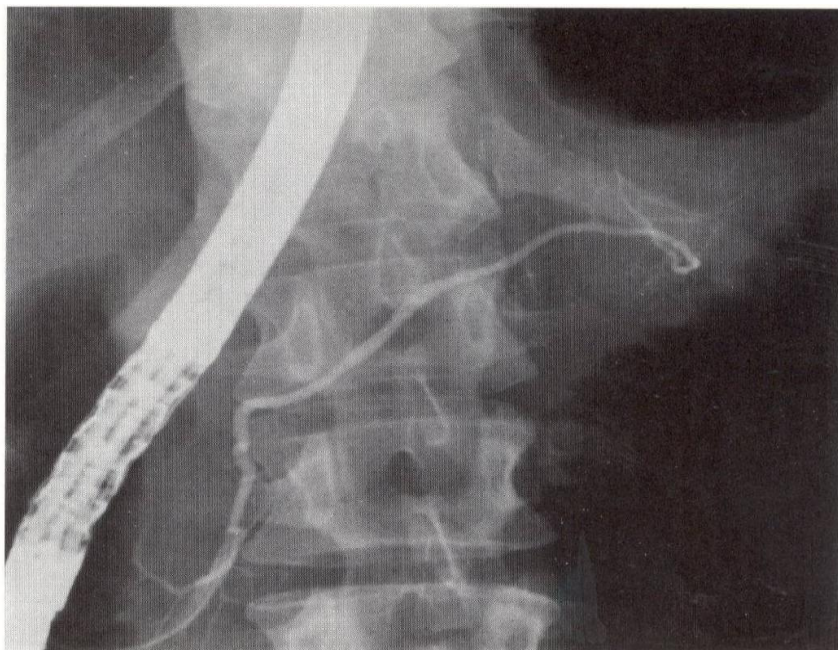
PANCREAS DIAGNOSTIC IMAGING

CLINICAL SKILLS

Self-assessment

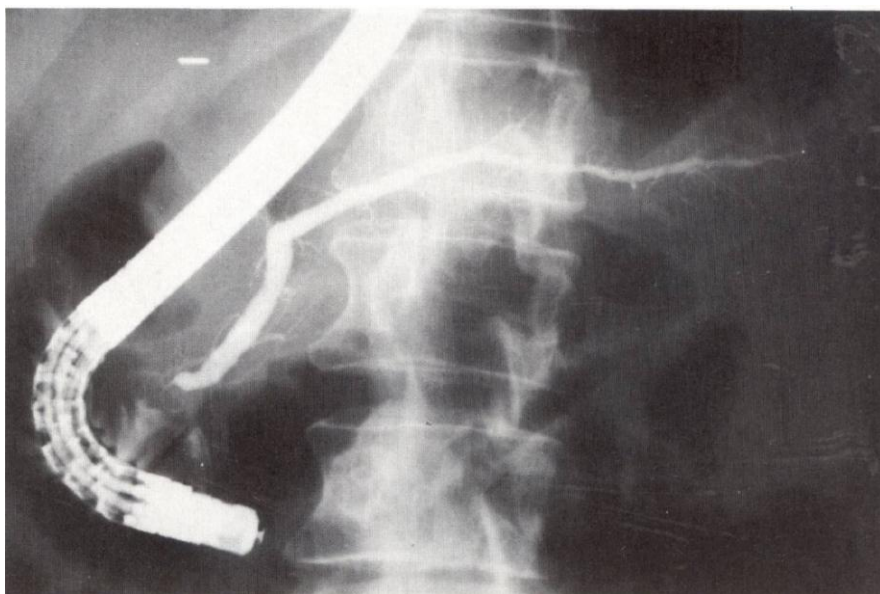
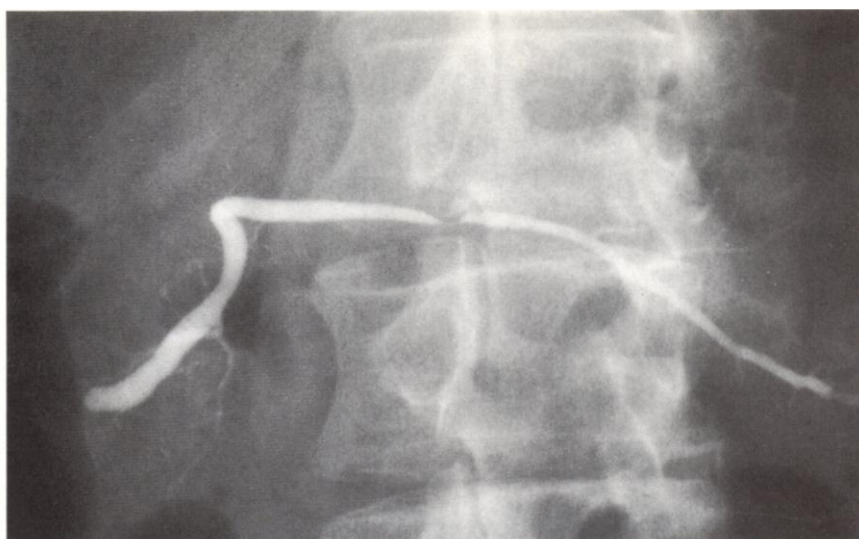
**Describe the findings, give a differential diagnosis,
and state the most likely clinical diagnosis.**

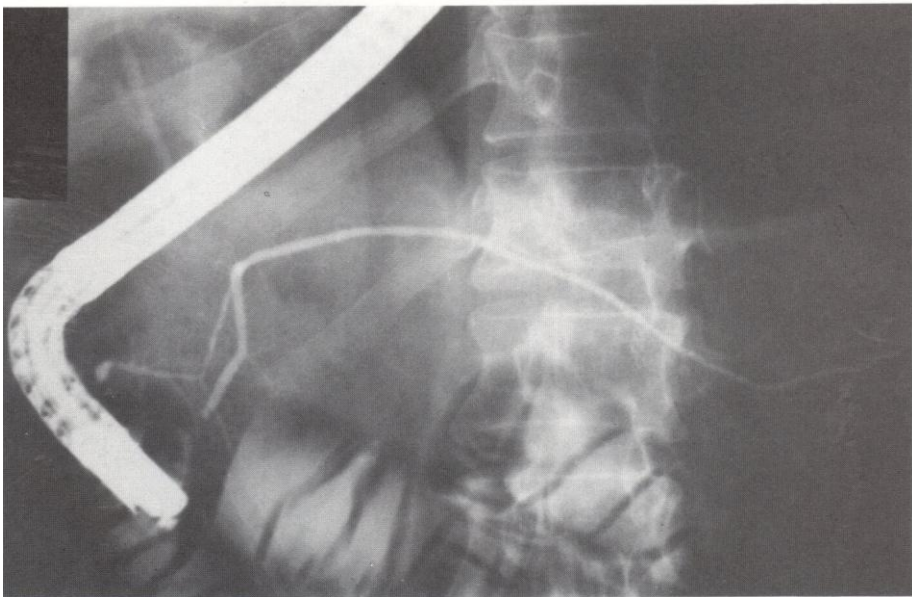
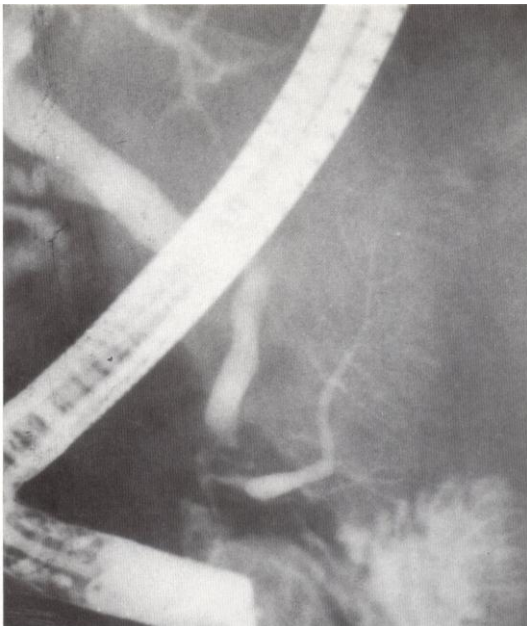


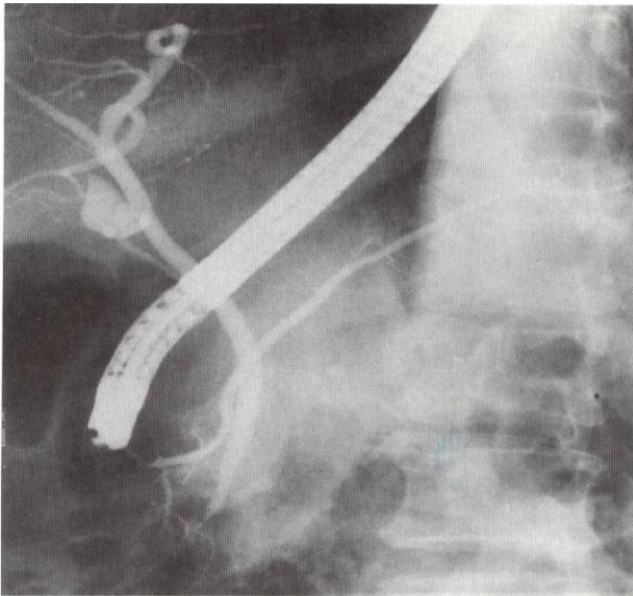
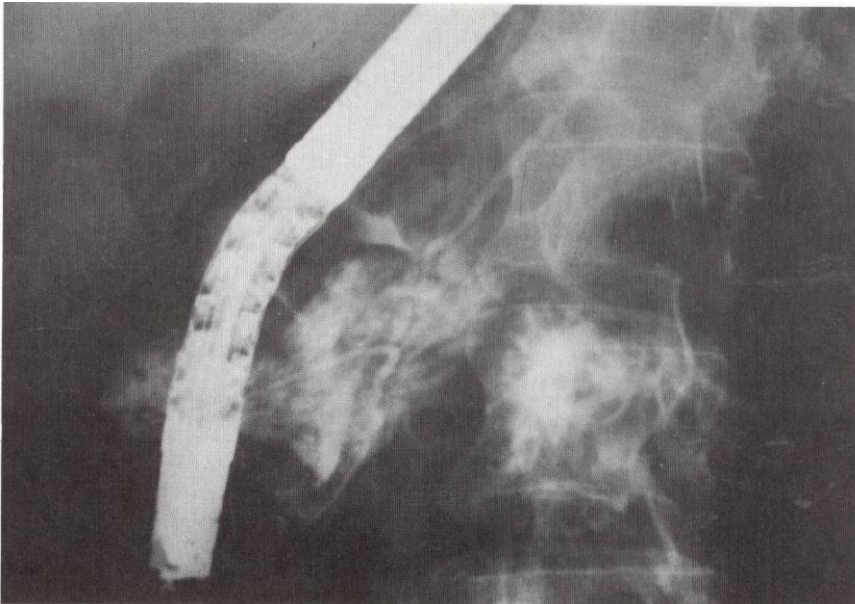
Case 1**Case 2**

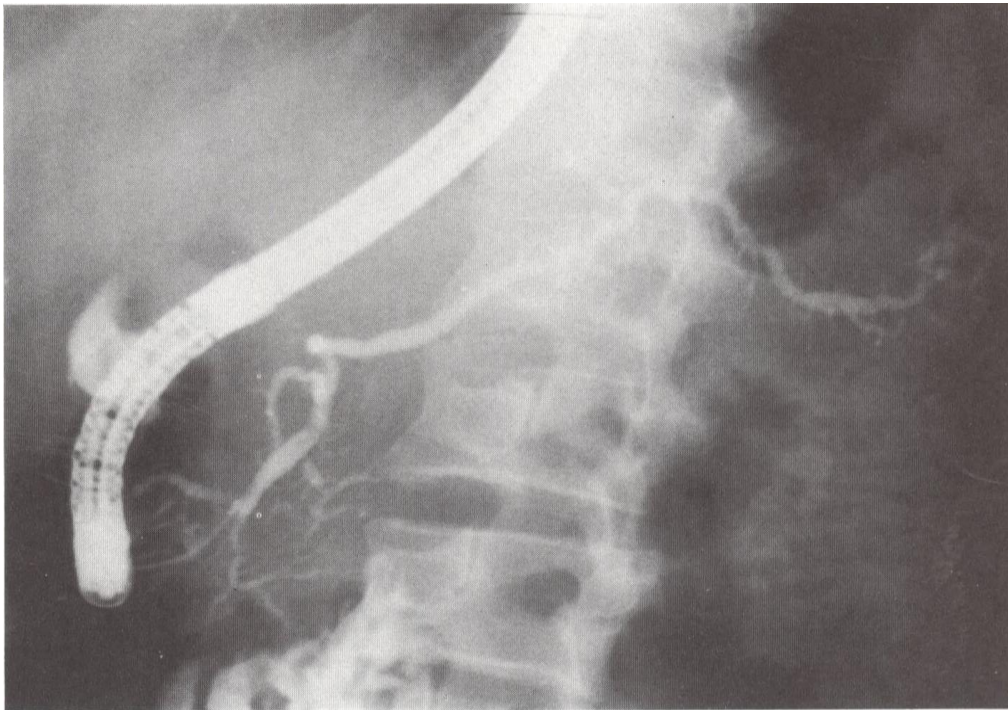
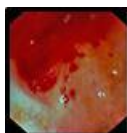
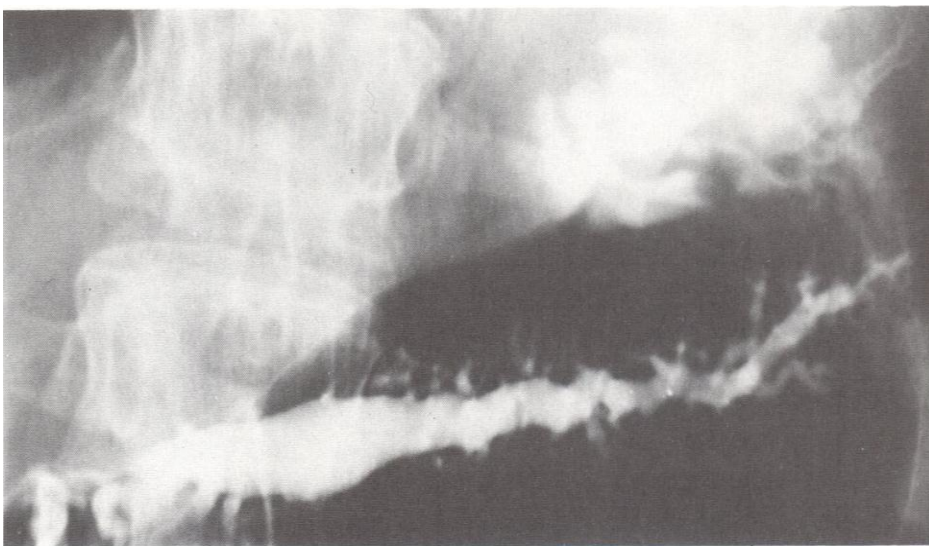
ENDOSCOPY and DIAGNOSTIC IMAGING

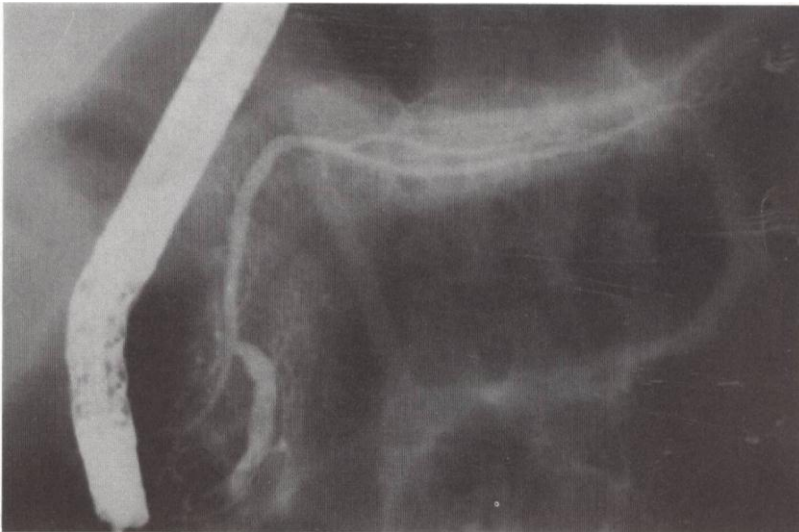


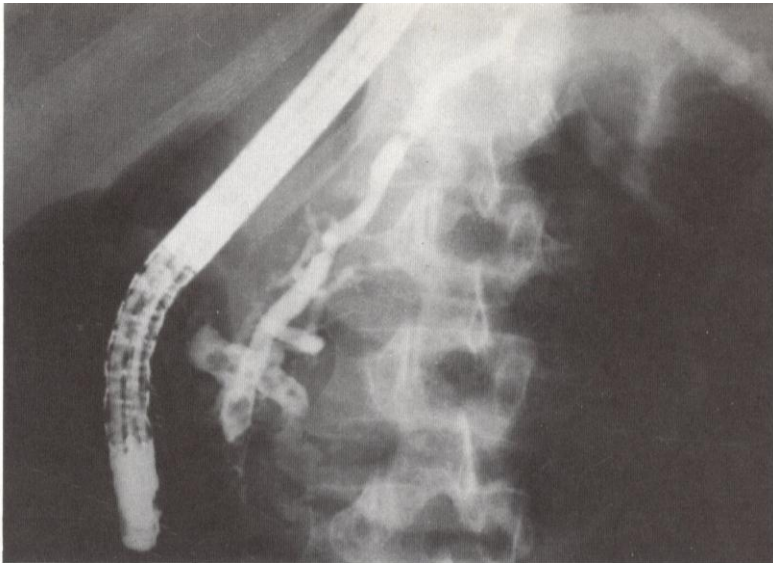
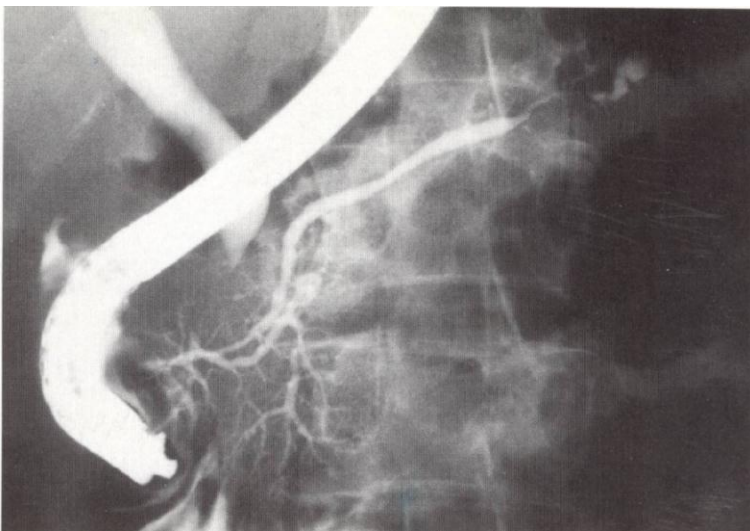
Case 3**Case 4**

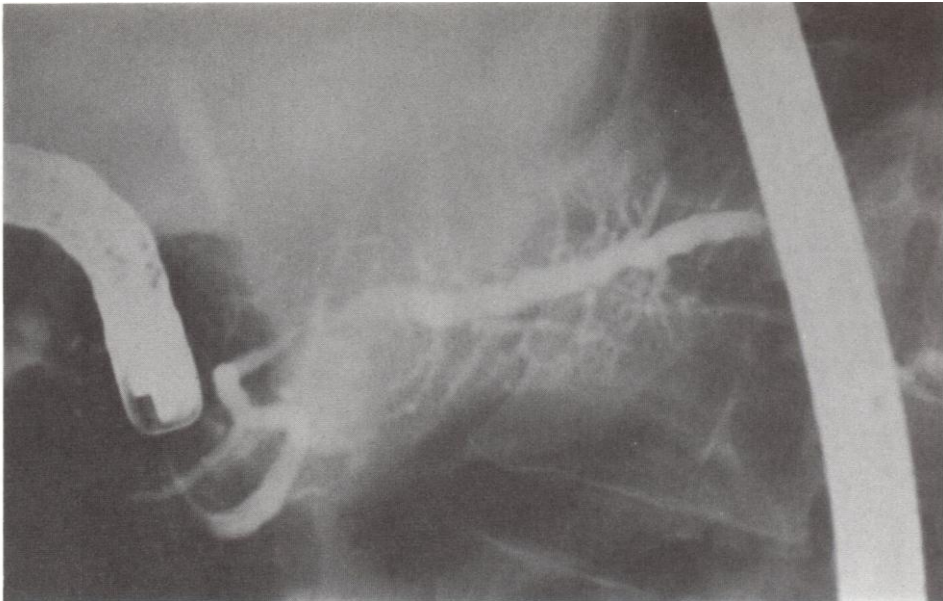
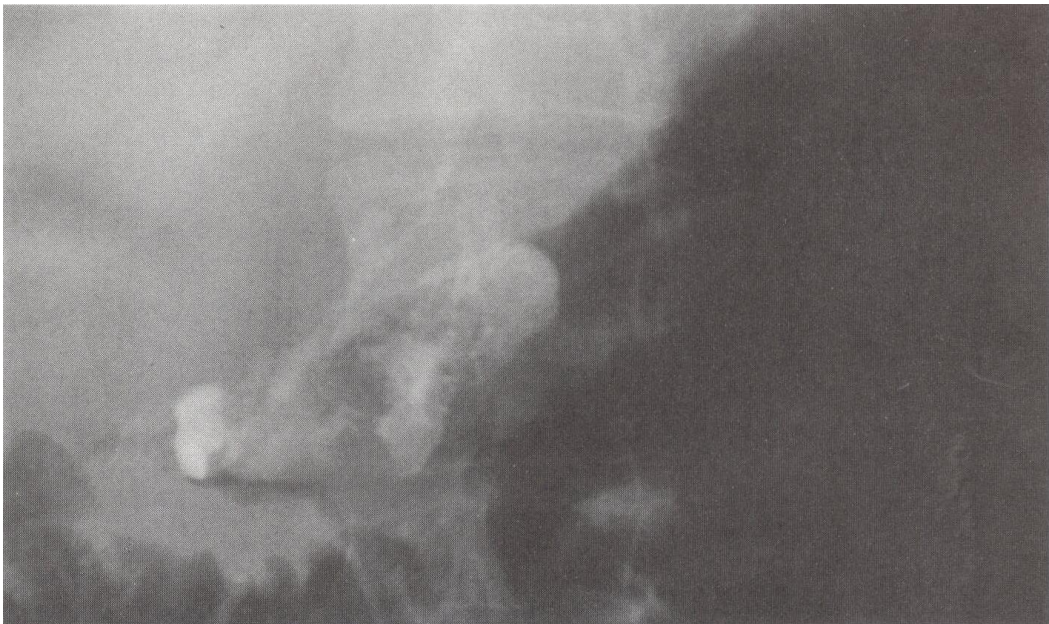
Case 5**Case 6**

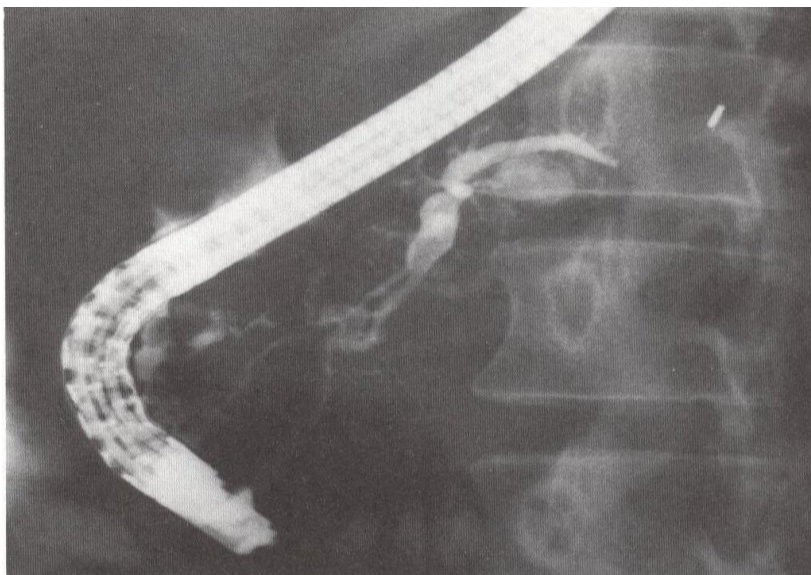
Case 7**Case 8**

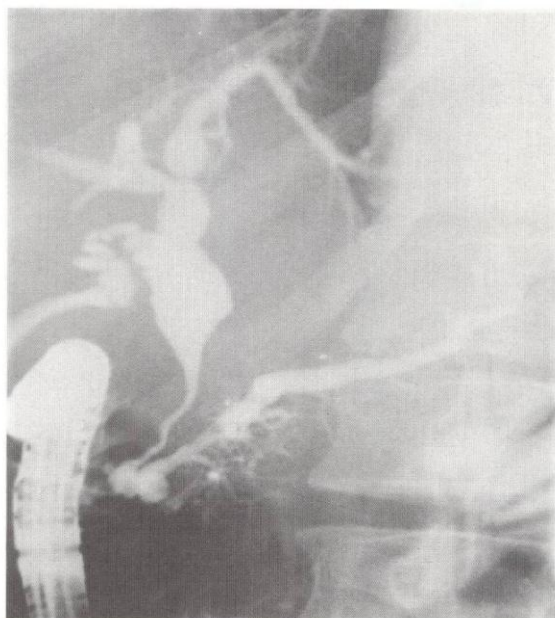
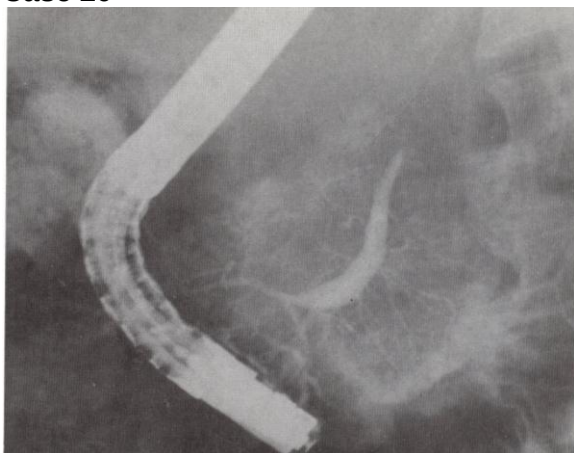
Case 9**Case 10**

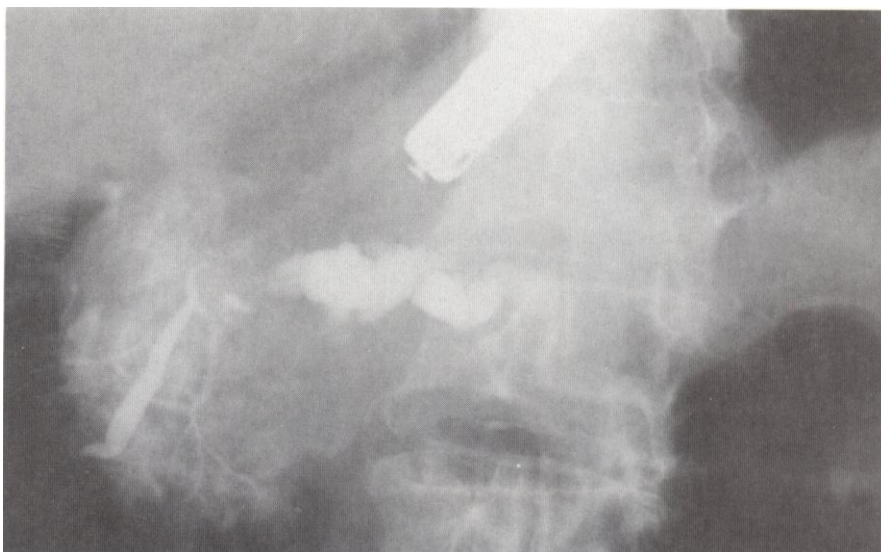
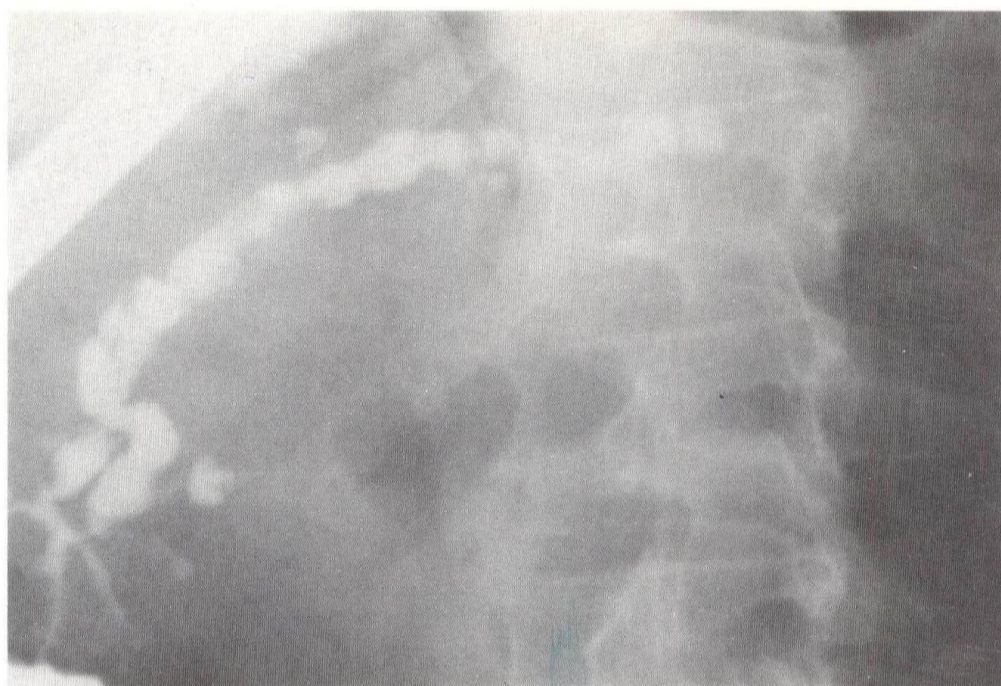
Case 11**Case 12**

Case 13**Case 14**

Case 15**Case 16**

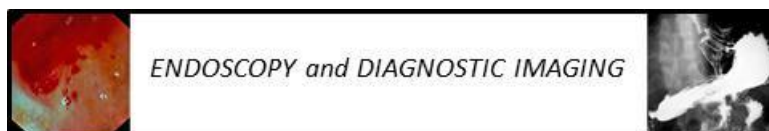
Case 17**Case 18**

Case 19**Case 20**

Case 21**Case 22**

Pancreas (ERCP) Answers

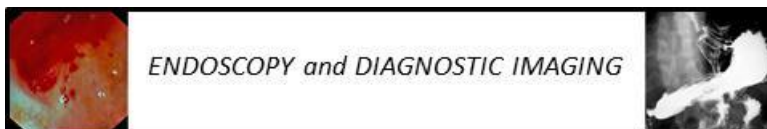
1. Normal pancreatic duct (<5 mm)
2. Normal pancreatic duct
3. Normal pancreatic duct
4. Narrowing of pancreatic duct : Underfilling of distal half, apparent narrowing Pseudostricture).
5. Filling of accessory duct of Santorini
6. Pancreas divisum
7. Pancreas divisum
8. Annular pancreas
9. Minimal change pancreatitis: Variations in duct calibre in tail, irregular branches, blobs of contrast in parenchyma.
10. Chronic pancreatitis: Dilated main duct, disorganized and dilated branch ducts, small cystic areas in parenchyma.
11. Chronic pancreatitis: Normal calibre ducts stopping suddenly in body of pancreas, with acinar filling in head and distal calcification.
12. Chronic pancreatitis: Bifurcation of main duct in body of pancreas, with calcification in parenchyma.
13. Calculi in pancreatic duct
14. Pancreatic pseudocysts: Pseudocysts at area of narrowing of duct at body/tail, as well as in the body itself.
15. Pancreatic abscess: Narrowing of duct in pancreatic neck, distal ductular dilation, contrast outside duct at area of narrowing.
16. Post ERCP after drainage of pancreatic duct: After drainage of duct of contrast material, with persistence of extravasated material (abscess)
17. Pancreatic abscess
18. Leaking pancreatic duct: Leakage of contrast just to the right of spine.
19. Narrowing of biliary system: Narrowing of proximal pancreatic duct, with smooth narrowing of distal common bile duct from fibrosis of head of pancreas from chronic pancreatitis.
20. Narrowing of pancreatic duct: Abrupt narrowing and blockage of pancreatic duct, with no signs of chronic pancreatitis (calcification, distal dilation, side branch changes); Compare with pancreas divisum in which the opacified portion of the duct is usually narrower.
21. Narrowing of pancreatic duct: Abrupt narrowing of pancreatic duct, but with distal dilation. The diagnosis was chronic pancreatitis, but here



there was no ductular changes in the head of the pancreas or calcification.

22. Carcinoma of the head of the pancreas: Entire pancreatic duct dilated by cancer in head of pancreas.

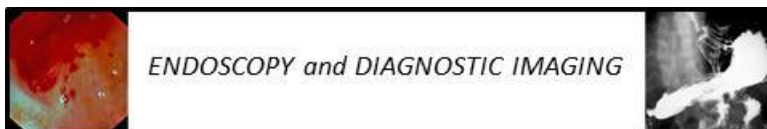
Please compare your findings with those described in the previous material.



For Your Consideration and Discussion:**ESOPHAGUS CLINICAL CASES**

1. Mr. S. L - 51 years old
GERD > 15 years
No "alarms"
EGD '06 biopsies BE+, EE+, no dysplasia, PPI bid; repeat
EGD EE-, BE+ (no dysplasia)
'07 colon – normal

2. Mr. K. B - 27 years old
Dysphagia L>S 3 years
PPI od minimal benefit
EGD n
Motility ↑ LES, Bernstein +
24 hour esophageal impedance normal
Biopsy - esophagitis, with eosinophils
Fluticazone 125 mcg bid swallowed; poor response



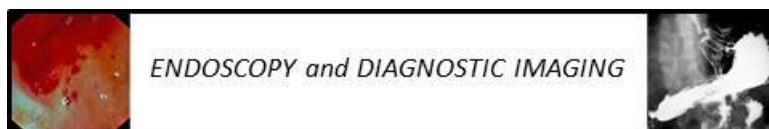
For your Consideration and Discussion:

STOMACH CLINICAL CASES

1. Ms. X. Y - 62 years old
 > 10 years GERD
 Recent incomplete relief with PPI od
 '05 Gastrectomy, R-en-Y
 Presents with disabling ↑ BM, cachexia

2. Mrs. A. B - 62 years old
 Long history of dyspepsia
 ↑ Ca, PTH – parathyroidectomy
 Persistent dyspepsia, EGD-DU, Hp+ - Rx
 ↑ gastrin
 Resection pancreas, tumor, MEN1
 Recurrent dyspepsia, ↑ BM (MBIG normal, chromogranin+,
 PET scan normal)
 ↑↑ gastrin
 Adrenal tumor, octreotide scan+

3. Mrs. M. M - 55 years old
 Years dyspepsia
 PPI + antidepressants – adverse effects
 Told she has a CYP-450 problem and to avoid Rx
 EGD N
 B, 42 CRC; father's brother, CRC age 51
 Colon N



For Your Consideration and Discussion:

SMALL INTESTINE CLINICAL CASES

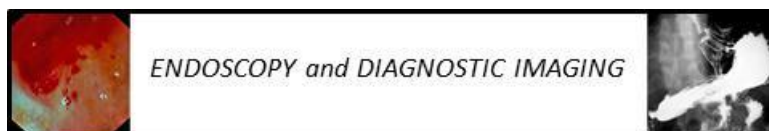
1. Mrs. A. S - 70 years old
 '83 DH, bx-celiac
 '89 abdominal pain, on gluten free diet – duodenal adenocarcinoma – Whipples procedure
 '08 Arizona Abd pain, CT- small bowel obstruction
 Colon, bx N, small bowel x-ray, N;, H2 breath test normal
 EGD SB biopsy – sprue

2. Ms. S. B - 40 years old
 CD-TI/C '85
 Pentasa® 6/Day
 Iron deficiency anemia - po Fe
 Hypothyroid Rx
 Colon '00 – Active CD
 Past use of CyA, No Im/MTX
 OCA +, smoke +, FH-CRC +

3. Mr. R. E - 31 years old
 '92 CD
 Duodenal + Crohn's, resection for obstruction
 Tissue transaminase neg, IgA N
 Prednisone 15g bid –taper – D/C –return of diarrhea
 3 months after prednisone – biopsy: subtotal villous atrophy, collagenous colitis

4. Mrs. T. M - 68 years old
 Recurrent iron deficiency anemia for > 20 years
 No alcohol, not a vegetarian
 81 mg ASA: DM; 4 brothers CAD
 EGD, colon N, SB X-ray N; biopsies SB, TI, colon N
 CE-multiple vascular ectasia of small bowel

5. Mr. A. S - 60 years old
 >20 years CREST syndrome dx 1980
 '97 EGD erosive esophagitis, PPI bid, dyspepsia, no dysphagia
 Loose stools, distention, H2 BT (lactulose) positive
 '02 colon RC 'TICS
 '09 LLQ pain, tenderness



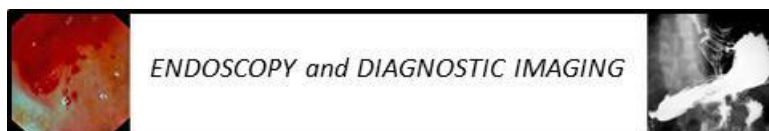
For Your Consideration and Discussion:

COLON CLINICAL CASES

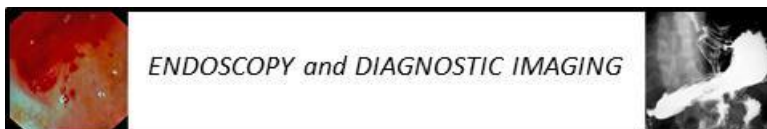
1. Mr. R. J - 69 years old
 Ulcerative proctitis '89
 Ankylosing spondylitis 30 yr
 Celebrex → naproxen
 GERD
 Depression
 DEXA N '01
 '96 sigmoidoscopy normal
 '99 sig' positive 0-2 cm
 Colon '01 – 0-8 cm, colitis, polyp 8 cm, hyperplastic
 TICS

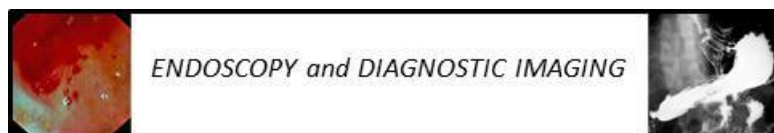
2. Mrs. M. L - 48 years old
 CRC Fam hx – Sister and 2 sons, brother 58, mother 42, 2
 maternal aunt – FAP, later confirmed genetically
 Subtotal colectomy for multiple colonic polyps, IR
 anastomosis, '90
 Recurrent rectal polyps
 Bx/removed q 6 mo, ASA/celebrex
 Total colectomy with IAPP'04
 '03 surveillance, duodenal adenomatous polyps plus fundic
 gland polyps – dysplasia – duodenectomy
 '05, more polyps, Whipples procedure
 DM, islet cell transplant
 '05 R. renal/ovarian cyst
 '05 uterus bulky on US – hysterectomy for Ca
 '06 mammogram bilateral cysts
 Fundic gland polyps (PPI +, Hp-), dysplasia '05, '06 – LGD,
 '07 – HGD
 Total gastrectomy: stricture at junction of esophagus &
 jejunum
 Nutritional risk

3. Mr. K. U - 56 years old – chronic diarrhea
 H2 breath test Lactulose+ –response to Flagyl
 Recurrence of diarrhea
 Colon TICS, bx – micro' colitis
 Pentasa® 2 g x2
 Diarrhea continues



4. Mr. L. R - 68 years old
'70 – CD-C
'79 Subtotal colectomy
'87 recurrence, prednisone
'97 - %=ASA po, pr
'87 – colon 30 cm NeoTI
'02 resection IAPP
'08 Recurrent diarrhea





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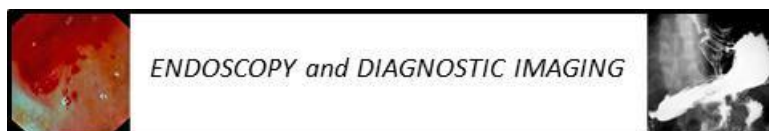
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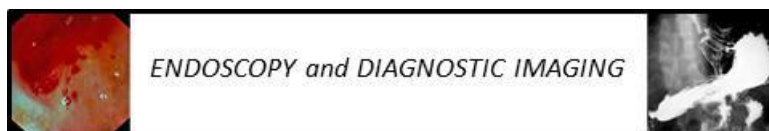
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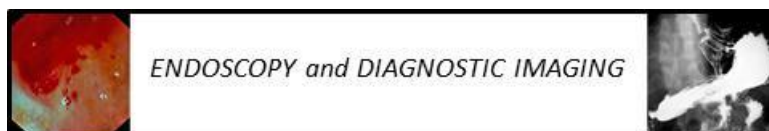
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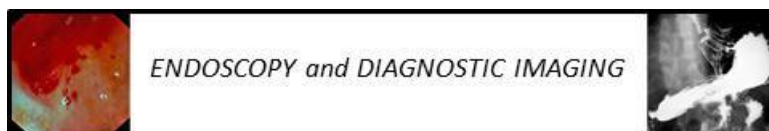
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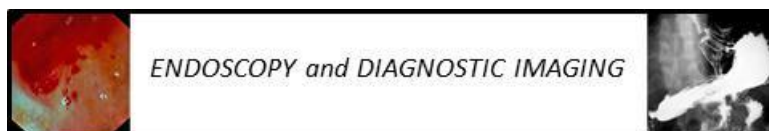
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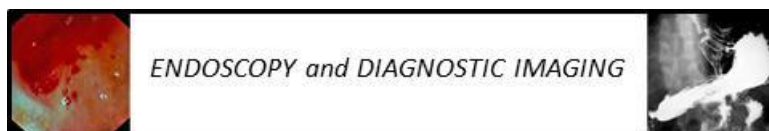
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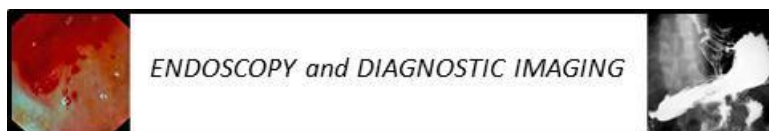
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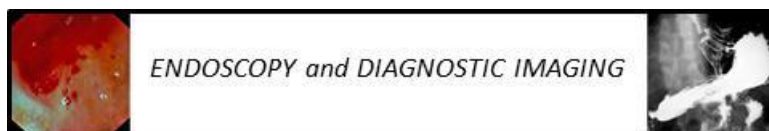
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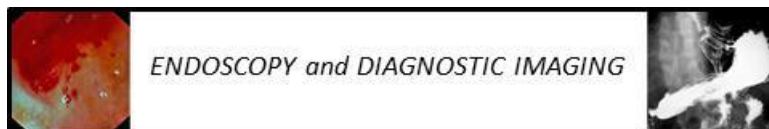
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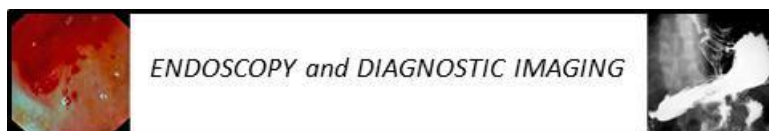
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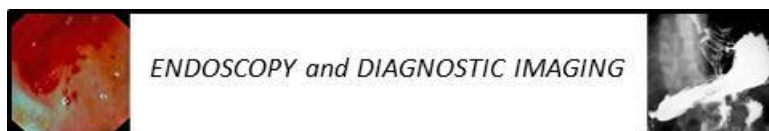
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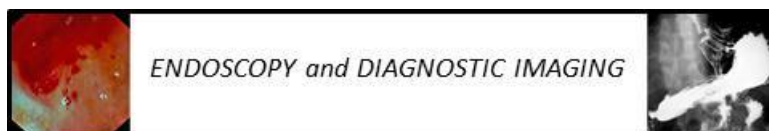
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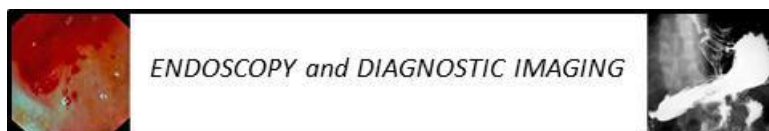
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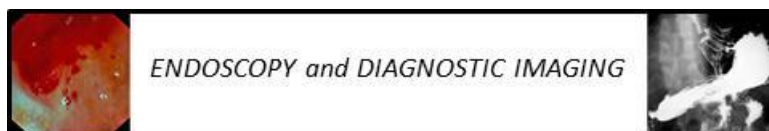
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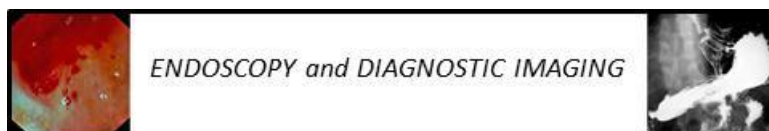
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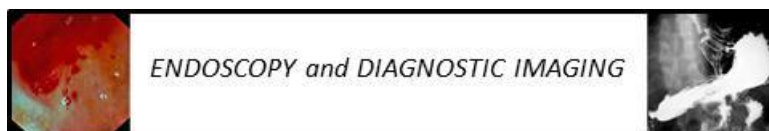
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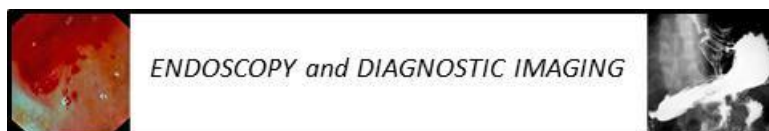
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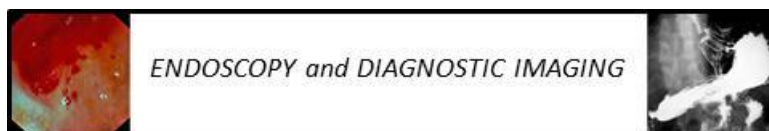
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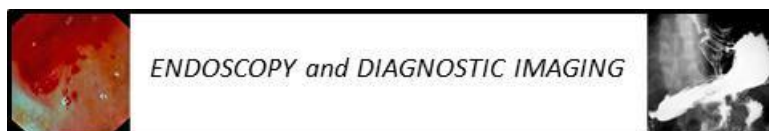
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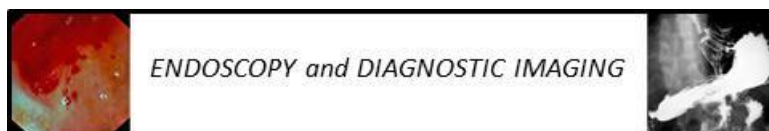
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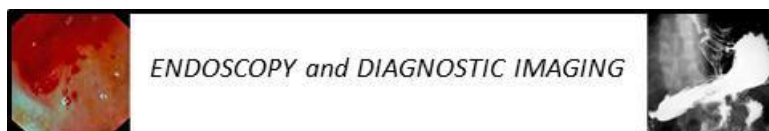
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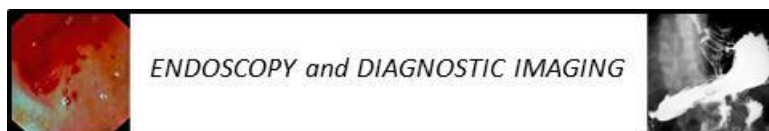
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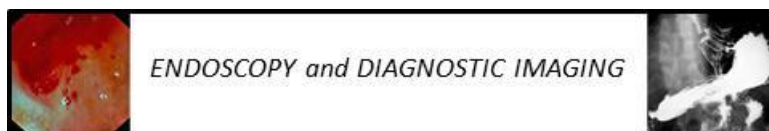
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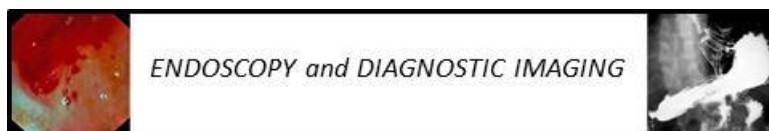
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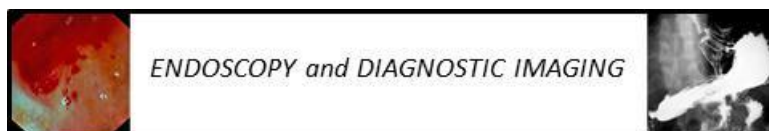
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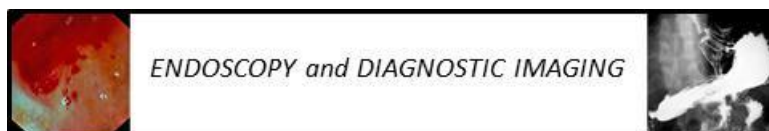
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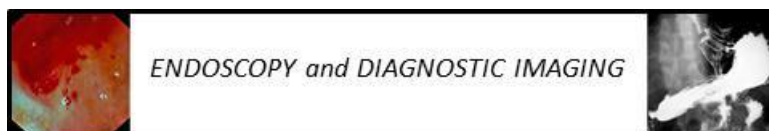
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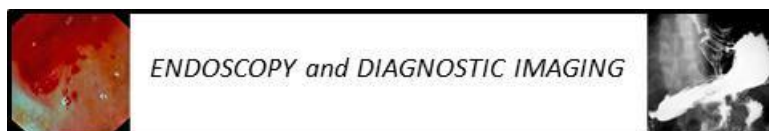
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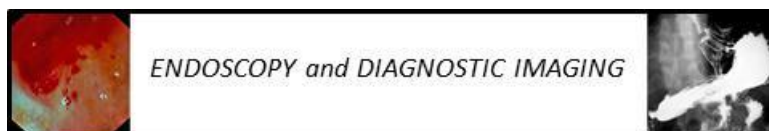
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